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SECONDARY TUMORS OF THE URETER

A CONSIDERATION OF THE VARIOUS TYPES, WITH A REPORT OF TWO CASES

CHAIRMAN'S ADDRESS

STANLEY R. WOODRUFF, M.D.
JERSEY CITY, N. J.

In the twelve years since the publication of a case report by Giordano and Bumpus [1] progressively increasing interest has been shown in secondary tumors of the ureters. The rarity of true metastasis to the ureter from adjacent pelvic organs, so often the seat of malignant disease, is difficult to explain when one remembers the frequency of occurrence of carcinoma of the bladder and the fact that the lymphatic vessels of the two organs communicate, unless one agrees with Robinson [2] that the lymphatic drainage of the lower portion of the ureters is downward. This is also true of other pelvic organs in both the male and the female. Even as rare a condition as primary carcinoma of the ureter appears to be, I am inclined to believe with Glas [3] that true metastases are even rarer, and it appears that the histologic structure of the ureter is somewhat immune to malignant invasion. Surely one must be impressed by the fact that a large number of the cases of true metastasis reported come from such rather remote organs as the breast, stomach and lung. My observations would force me to believe also that there are many metastases to the ureter that are entirely missed because of their small size and the lack of symptoms. The most frequent metastatic growths of the ureter are really inoculation or implantation metastases from an original papillary carcinoma of the renal pelvis.

CLASSIFICATION

In order to clarify these conditions I have endeavored to formulate a classification of secondary tumors of the ureter based on pathogenic principles.

I. Involvement of the ureters by the urogenic route.
  (*a*) In the direction of the urinary flow (from the kidney or pelvis).
  (*b*) Retrograde (from the bladder).

II. Involvement of the ureter by direct extension from a neighboring viscus.
  (*a*) Encircling the ureter without infiltration of the ureteral wall.
  (*b*) With infiltration of the ureter.
    1. Without encroachment on the lumen.
    2. With encroachment on the lumen.
    3. With subsequent rupture into the ureteral lumen.
      (*a*) Further dissemination by the urogenic route (as in group I).
    4. With subsequent invasion of the blood or lymph channels (acting as a supplementary focus for further dissemination).

III. Involvement of the ureter by the blood or lymph channels (genuine metastases).

IV. Combination form (combination of any of the former).

V. Involvement of the ureter by lesions that may be of multicentric origin.
  (*a*) Diseases of the hematopoietic system.
    1. Hodgkin's disease.
    2. Lymphosarcoma.
    3. Leukemia.
    4. Reticulosis.

GROUP I: *Involvement of the Ureter by the Urogenic Route.*—(*a*) Clinicians are fully cognizant of the tumors that arise in the renal pelvis and metastasize down the ureter by way of the urinary stream. Such implantation may continue onward into the bladder, where papillary tumors grow with great facility. This condition has been demonstrated to be so common that urologists now feel it necessary to make a thorough study of the ureter and renal pelvis by the usual methods in every patient showing papillary growths in the bladder. Albarran [4] first brought attention to the ease with which papillary tumors of the renal pelvis can become implanted in the mucosa of the bladder. Hunt [5] in 1927 reported fifteen cases of papillary epithelioma of the renal pelvis, which series was later covered by Kimball and Ferris [6] in their recent (1934) review of the literature in connection with such tumors. They collected reports of seventy-four cases, in fifty of which metastases appeared in the ureter and bladder. In only one of these cases does it appear that the ureter alone was the subject of metastatic implantation, but in twenty-four cases, or 48 per cent, the ureteral orifices were involved, while in eighteen cases, or 36 per cent, both the ureteral orifice and the bladder showed papillary tumors. Cabot and Allen [7] in 1933 reported forty-five cases, nineteen of which were also included in the data of Kimball and Ferris. In the remaining twenty-six cases there were seven metastatic implantations in the ureter. The accepted procedure in operating on a patient suffering from papillary carcinoma of the renal pelvis now includes total extirpation of the ureter along with a portion of the vesical wall, even in those patients

Read before the Section on Urology at the Eighty-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 14, 1935.

From the Department of Urology, Bayonne Hospital and Dispensary, with the collaboration of the Department of Pathology, William Antopol, M.D., director.

1. Giordano, A. S., and Bumpus, H. C.: J. Urol. **8**: 445 (Nov.) 1922.
2. Robinson, A., cited by Cunningham, D. J.: Textbook of Anatomy, 1923, p. 1026.
3. Glas, Richard: Wein. klin. Wchnschr. **39**: 1145 (Sept. 30) 1926.
4. Albarran, J.: Ann. d. mal. d. org. génito-urin. **18**: 701, 1900.
5. Hunt, V. C.: J. Urol. **18**: 225 (Sept.) 1927.
6. Kimball, F. N., and Ferris, H. W.: J. Urol. **31**: 257 (March) 1934.
7. Cabot, Hugh, and Allen, R. B.: Lancet **2**: 1301 (Dec. 9) 1933.

in whom no secondary growth of the ureter or bladder can be demonstrated. Metastasis of the ureter from the renal pelvis appears to take place by the actual adherence of tumor cells to the mucosa, with subsequent implantation on it as they float down in the stream of urine, and not by lymphatic or adjacent growth.

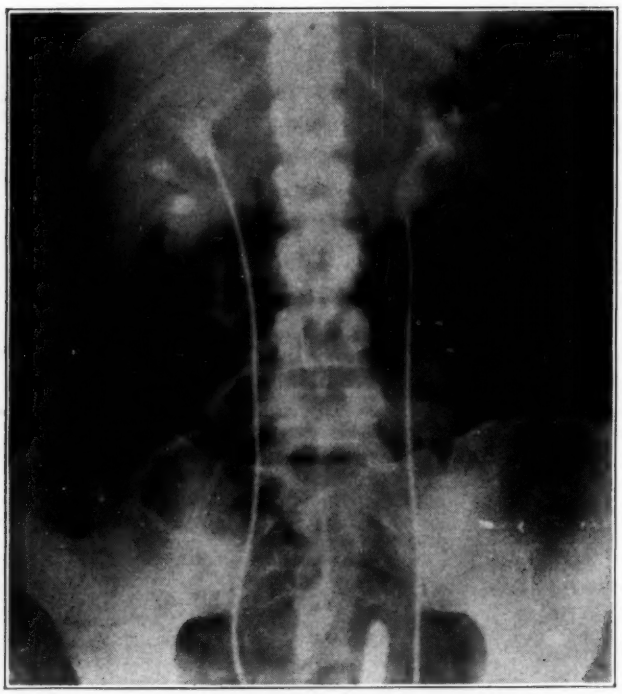

Fig. 1.—Pyelogram with the catheters in place.

(*b*) Retrograde dissemination of neoplasms upward was mentioned by Ewing.[8] He described several papillary tumors of the bladder which extended into the lumen of the ureter. Boeger's[9] patient died two years after resection of the sigmoid flexure for carcinoma. At necropsy a tumor was found in the left ureter, with dilatation of the ureter and pelvis above it. There was carcinomatous involvement of the medulla of the kidney and pelvis. In this case the author believed that the patient had metastases at the bifurcation of the aorta at the time of operation, and that these tumors grew into the adjacent tissues, invaded the ureter, broke into the lumen and then gave rise to renal and pelvic implants by the retrograde urogenic route. The ureter above and below the constriction was found to be uninvolved in the tumor process.

GROUP II: *Involvement of the Ureter by Direct Extension from a Neighboring Viscus.*—(*a*) That the ureters may be embedded in adjacent extra-ureteral tumors without actual invasion by them was shown in Martin's[10] case of primary carcinoma of the cervix with metastasis to the vagina. The ureter in this instance was completely encircled by tumor tissue for a distance of 2 cm. In spite of this the ureter could be easily freed from the tumor, the latter being removed at operation. The ureteral wall was found to be free of invading tumor tissue.

The literature is full of reports in which pressure on the ureter by an adjacent tumor has been the cause of marked changes in the ureter, the result of stricturization of the ureter usually being ureterectasis and pyelectasis, which is commonly followed by infection resulting in pyonephrosis and destruction of the kidney. Herger and Schreiner[11] reported twenty-one such cases in a series of autopsies on thirty-two patients who died of carcinoma of the cervix.

(*b*) 1. More aggressive tumors adjacent to the ureter may, however, infiltrate its wall with or without interference with the lumen. In Maruyama's[12] first case the lumen was not obliterated even though the wall was infiltrated.

2. In Myers'[13] patient anuria developed thirty days before death, about four months after hysterectomy for carcinoma of the cervix. At necropsy both ureters were found to be incarcerated in a pelvic mass which had already infiltrated the ureteral walls and occluded the lumens.

3. After the tumor has invaded the ureteral wall, it may rupture into the lumen and then spread by the urogenic route to other portions of the ureter, to the bladder or retrograde to the pelvis and kidney (as in Boeger's case described in group I).

4. After the tumor has invaded the ureteral wall, this secondary tumor may act as a supplementary depot for further dissemination by way of the lymph or the blood stream. In Maruyama's[12] first case there was a large mass in the pelvis extending from a carcinoma of the cervix. The left ureter was invaded and embedded in this mass, but its lumen was not obliterated. The lymphatic vessels extending up to the ureter were infiltrated by tumor tissue. In this instance it is difficult to decide whether the lymphatic extension was from the pelvic mass or from the involved ureter. The second source, however, is more likely.

Fig. 2.—Uterus, cervix and vagina, showing an ulcerated lesion of the fornix extending into the vagina and encroaching on the cervix.

GROUP III: *Involvement of the Ureter by the Blood or Lymph Channels (Genuine Metastases).*—The first to stress invasion of the blood stream by tumor cells

8. Ewing, James: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1922.
9. Boeger, Alfred: Beitr. z. path. Anat. u. z. allg. Path. **80:** 640 (Oct. 5) 1928.
10. Martin, J. F.: Lyon méd. **117:** 535, 1911.
11. Herger, C. C., and Schreiner, B. F.: Surg., Gynec. & Obst. **43:** 740 (Dec.) 1926.
12. Maruyama, Ichiro: Okayama-Igakkai-Zasshi **40:** 1087, 1928.
13. Myers, W. A.: Obstructive Anuria, J. A. M. A. **85:** 10 (July 4) 1925.

were Giordano and Bumpus in 1922.[1] They reported a case in which there was a carcinoma of the prostate with metastasis to the left ureter. In 1924 Thomas and Regnier [14] reported a case of carcinoma of the bladder with metastases to the right ureter. They made no mention of perivascular lymphatic vessels, merely stating that the cervical, inguinal and mesenteric lymph nodes were involved. Carson [15] in 1925 stressed invasion of the lymphatic vessels, reporting three cases, one from the bladder, another from the prostate and a third from the cervix. In 1927 Carson [16] described two additional cases that fall into this group, both from the prostate.

Fig. 3.—Section under low power showing ulcerated lesion with invasion of deeper tissues by pegs of tumor cells.

Rathbun [17] in 1929 reported a case in a male occurring three years after mastectomy for carcinoma. Urinary symptoms developed at that time and a urologic examination established the diagnosis of renal tumor, probably carcinoma. Excision of the left kidney and partial ureterectomy were performed and a tumor nodule, having the characteristics of the original breast tumor, was found in the wall of the ureter. The author made no mention of lymphatic extension, but that was undoubtedly a case of true metastasis.

Kirshbaum [18] reported five cases of involvement of the ureters, the first subsequent to mastectomy for carcinoma, the third secondary to bronchial carcinoma and the fourth and fifth originating in prostatic carcinomas. His second case was one of Hodgkin's disease, which will be included in a special group.

In considering the cases of true metastasis to the ureter, one must not be overcautious and include only those instances in which tumor is present within the lymph or blood channels. In the first place it is not uncommon to find a lymph node involved in a tumor process without demonstration of neoplastic tissue within the afferent or efferent channels. Indeed, one would be compelled to make serial sections, and even then the cells would not necessarily be demonstrated. This is particularly so in those cases of infrequent sporadic invasion in which the cells are immediately propelled through the lymph vessels without involving either intermediate lymphatic gland or the very channel through which it traveled to its new nidus. Furthermore, in those cases in which the lymphatic vessels are found to be actually involved it might well be an efferent vessel, as in Maruyama's first case, since one cannot differentiate an afferent from an efferent lymphatic channel. Again, supposing these could be differentiated, the possibility of retrograde involvement must necessarily be considered.

Therefore, all cases in which the ureteral involvement is not in direct continuity with the primary or adjacent tumor, even though actual invasion cannot be demonstrated, should be considered as possibly falling into this group.

In Grenel's [19] case of carcinoma of the lesser curvature, both ureters were dilated at the pelvic brim, where they were found to be infiltrated by carcinomatous tissue. The corresponding nodes at the points of obstruction were found to be involved in the tumor process, but they did not compress the ureter in those areas. This case evidently falls into the group of cases emphasized in this paper, even though the tumor cells were not found within the lumen of the lymphatic channels; otherwise one could not explain the migration of neoplasm from the ureter to the corresponding lymph node, or vice versa.

There are numerous other cases which in all likelihood border on or belong in this group, although no direct mention of this is made in the presentation.

Fig. 4.—Kidneys, ureters and bladder. The ureters are thickened and infiltrated.

Zinner [20] reported a case in which hysterectomy was performed for columnar cell carcinoma of the uterus two and one-half years before the patient's death. At necropsy, tumor nodules were found in the right ureter 5 cm. below the ureteropelvic junction and in

14. Thomas, G. J., and Regnier, E. A.: J. Urol. **11**: 205 (March) 1924.
15. Carson, W. J.: Ann. Surg. **82**: 142 (July) 1925.
16. Carson, W. J.: Ann. Surg. **86**: 549 (Oct.) 1927.
17. Rathbun, N. P.: J. Urol. **21**: 507 (April) 1929.
18. Kirshbaum, J. D.: J. Urol. **30**: 665 (Dec.) 1933.
19. Grenel, Walter: Ztschr. f. Urol. **14**: 393, 1920.
20. Zinner, A.: Ztschr. f. urol. Chir. **17**: 369, 1925.

the left ureter 4 cm. above the orifice. Those nodules were apparently metastatic and not in connection with the remnants of primary tumor tissue.

Bauer [21] in discussing this case mentioned one of his own cases, that of a man, aged 50, with carcinoma of the stomach and metastasis to the left ureter.

Case 3 in Glas's [3] series is a more complete report of Bauer's case. Glas's second case was one of carcinoma of the prostate in a man, aged 74, with involvement of the lymph nodes and lower third of both ureters. An isolated node in the left ureter, together with involvement of the regional lymph nodes, was found. In his fourth case, a woman, aged 50, had one breast amputated for carcinoma fifteen years before death and an ovarian carcinoma removed two years before death. At necropsy, metastatic carcinoma of the

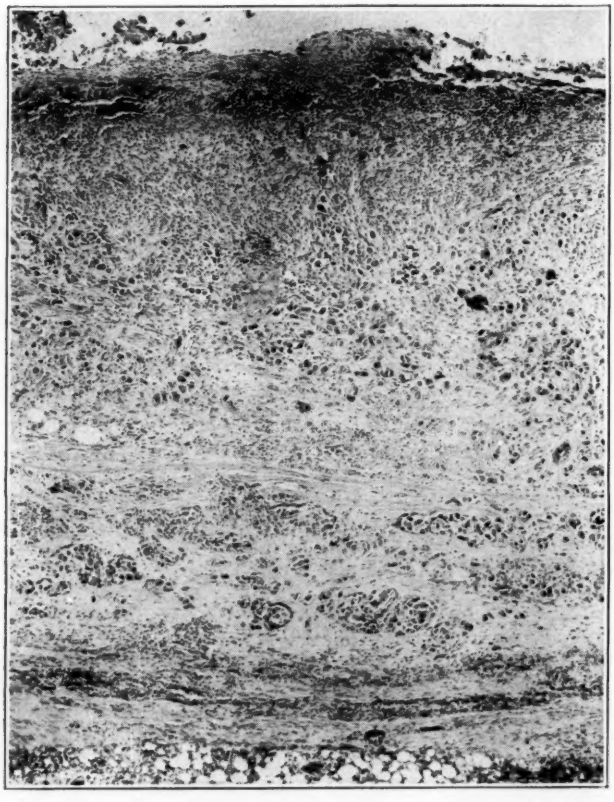

Fig. 5.—Section of the ureteral wall under low power showing intact but inflamed mucosa and the infiltration of the muscular coat and perimuscular areas by tumor tissue. Note the increase in connective tissue about the neoplastic areas.

inguinal and retroperitoneal lymph nodes with infiltration of both ureters was found.

Eisner [22] reported the case of a 45 year old man with pulmonary tuberculosis, pernicious anemia and carcinoma of the stomach. In the perirenal tissues there were tumor masses which encroached on the ureters. He mentioned the possibility of lymphatic spread but did not specifically state that his case belonged to that group. His second case of carcinoma of the stomach, in which there were metastases to the peritoneum, ovaries, bladder and right ureter, may also fall into this group.

MacKenzie and Ratner [23] reported three cases of true metastases to the ureter. In two cases autopsy was performed. In one case a diagnosis was made prior to operation and represents practically the only case under this heading in which a preoperative diagnosis has been made. In the first case there was metastasis to the right ureter and ileum from an adenoscirrhous carcinoma of the stomach. It had caused pyonephrosis of the right kidney. The second case was one of adenocarcinoma of the prostate with metastases to the ureters, lungs and pleurae. The finding of cancer cells in the perivascular lymph spaces definitely proved the true metastatic nature of the growth. Pyonephrosis of the right kidney also was present. The third patient was suffering from carcinoma of the cervix and had been given radium treatment. Examination about a year afterward failed to reveal any recurrence of the growth. However, on admission to the hospital at that time she complained of frequency of urination and pain in the left iliac region, anorexia and loss of weight. This condition had been present for about four months. Urologic examination led to a diagnosis of ureteral obstruction and an infected pyelectasis of the left kidney. Excision of the left kidney and partial ureterectomy were performed. A congenital anomalous kidney was found with a double pelvis and two ureters which anastomosed in the upper third. At their junction was a hard mass the size of a large grape. It was removed along with the kidney and upper portion of the ureters. Pathologic examination showed this mass to be a metastatic carcinoma from the cervix.

GROUP IV: *Combination Forms.*—It is obvious that any combination of the aforementioned types of metastases may exist, and it is not necessary to give any details of cases.

GROUP V: *Involvement of the Ureter by Lesions Which May Be of Multicentric Origin.*—(*a*) It is not infrequent to find ureteral involvement in cases of tumor of the hematopoietic system. These tumors may arise in situ from the resting mesenchyme or from reticular cells.

Kirshbaum's [18] instance of Hodgkin's disease falls into this group. Bond Stow's [24] case of fibrolymphosarcoma of both ureters, which he considered secondary to lymphosarcoma of the anterior mediastinum, is most likely one of this variety. He reported that all the lymph nodes were involved. This was in all likelihood a case of lymphosarcoma.

A 14 year old girl with subleukemic myelosarcoma involving the heart, stomach, appendix, ovaries, tubes, ureters, kidneys, bladder, liver and all the lymph nodes with nodes in both ureters, which gave rise to obstruction with dilatation of the ureter and pelvis, was admitted to the hospital, because of nodules in the skin and asthenia with progressive anemia. Under observation, new nodules occurred in the skin and in the breasts. The liver became enlarged, as did also the spleen. The patient finally died. Within the ureters were seen numerous nodular infiltrations, varying from 2 to 8 mm. in diameter, which in places completely occluded the lumen of the ureter. The pelvis and terminal calices were dilated, and infiltrations were seen between the pelvis proper and the medullary portion of the kidney.

Even though no case has been reported in which reticulosis of the ureters was present, this is a likely possibility and is added for the sake of completeness of the classification.

21. Bauer, T. H.: Ztschr. f. urol. Chir. **19:** 370, 1925.
22. Eisner, Fritz: Med. Klin. **24:** 1237 (Aug. 10) 1928.
23. MacKenzie, D. W., and Ratner, M.: Canad. M. A. J. **25:** 265 (Sept.) 1931; Brit. J. Urol. **4:** 27 (March) 1932.
24. Stow, Bond: Ann. Surg. **50:** 901, 1909.

SYMPTOMATOLOGY

It is apparent to the urologist that the symptoms resulting from secondary tumors of the ureter vary according to the amount and type of the invasion. No doubt there are many instances in which no symptoms develop, and it stands to reason that many cases probably remain unnoticed. If there is little or no pressure on the ureteral lumen, only slight symptomatology will result, but with the advent of obstruction and probable later infection, the complaint will follow the usual course of such conditions. The extent and type of renal involvement will determine the symptoms, as they will in all probability relate to the pathologic condition of the kidneys, and the presence of ureteral complication will be difficult to determine. Pain in the back as an early symptom was noted in almost all the cases that have been reported, and was present in my own case. Sudden and complete anuria, as occurred in my patient, is extremely rare, but was noted by Schlagintweit.[25] He described a case in which this symptom developed and at autopsy bilateral metastatic carcinosis of both ureters from primary carcinoma of the stomach was discovered. Usually the patient shows only the symptoms relative to ureteral obstruction, such as pyelectasis, with or without infection.

The case to be presented here belongs in the third group—cases of true metastases. This case is interesting not only from the standpoint of the rare pathologic observations, but also because of the peculiar symptoms, which made diagnosis impossible and thereby caused the treatment to be mostly expectant.

REPORT OF CASE

History.—H. C., a white woman, aged 42, on admission to the hospital complained that no urine had been passed for six days. During that time there were two attacks of chills accompanied by fever. She also complained of nausea and vomiting and some lumbosacral backache. Her present illness began about one month previous to admission. While reaching for a telephone, she was suddenly seized with a pain in the lower portion of the spine. At first severe, it gradually subsided until a rather dull constant ache remained. She received medical attention at that time and was treated by several physicians for lumbago. During that time there were no genito-urinary symptoms. There was no history of any recent infectious disease.

Physical Examination.—The temperature was 102 F.; the pulse rate, 116, and the respiratory rate, 20. The patient appeared to be seriously ill and toxic. Nothing of particular interest was elicited by physical examination except the following: The abdomen was slightly distended but was soft and showed no masses or areas of tenderness. Pelvic examination revealed an ulcerated area in the vagina, which was palpated by the finger. In view of the fact that it was not particularly indurated and showed no connection with any underlying organ, it was considered to be of no great significance as far as the chief complaint was concerned. The regions of the kidneys showed no particular tenderness or rigidity. The reflexes were not abnormal. There was no edema. The blood pressure was 204 systolic and 120 diastolic.

Laboratory Examinations.—Chemical examination of the blood revealed 100 mg. of urea nitrogen per hundred cubic centimeters and 8 mg. of creatinine. The blood count showed 16,200 leukocytes with 84 per cent polymorphonuclears. The hemoglobin content was 60 per cent.

When the patient entered the hospital, catheterization was attempted but no urine was found in the bladder. Roentgen examination of the genito-urinary tract revealed that both kidneys were normal in shape, size, position and density. No evidence of calculous disease could be demonstrated at any point in the urinary tract. Cystoscopic examination showed that there was no urine in the bladder and that all the mucosa had a normal appearance. A catheter was passed to the pelvis of the right kidney without difficulty and 150 cc. of urine was obtained in a short time. An unsuccessful attempt was made to pass a number 5 catheter up the left ureter, but as the patient's condition became somewhat alarming it was decided not to make a further attempt. The urine from the right kidney contained a few white blood cells, many red blood cells, no casts and 1+ albumin.

Course.—During the next twenty-four hours the patient had several chills, the temperature rising to 103 F. along with a pulse rate ranging from 120 to 140. The output from the catheter in the pelvis of the right kidney was 2,700 cc. This catheter became blocked during the afternoon and could not be freed. After removal of the catheter, no urine passed into the bladder. Cystoscopy was again performed and the right kidney was catheterized, 150 cc. of slightly cloudy urine being obtained from the pelvis. The pelvis of the left kidney was successfully catheterized on this occasion and 75 cc. of clear urine obtained.

Bilateral delineation of the renal pelves with the aid of a contrast medium was carried out, the result showing that the pelvis of the left kidney was normal, while that of the right kidney was a trifle dilated. Unfortunately, the catheters were not removed from the pelves when the pyelogram was made, so that delineation of the ureters was not accomplished (the cystoscopist was loath to remove the catheters after having successfully placed them in the renal pelves). The urine obtained from the two kidneys was practically identical.

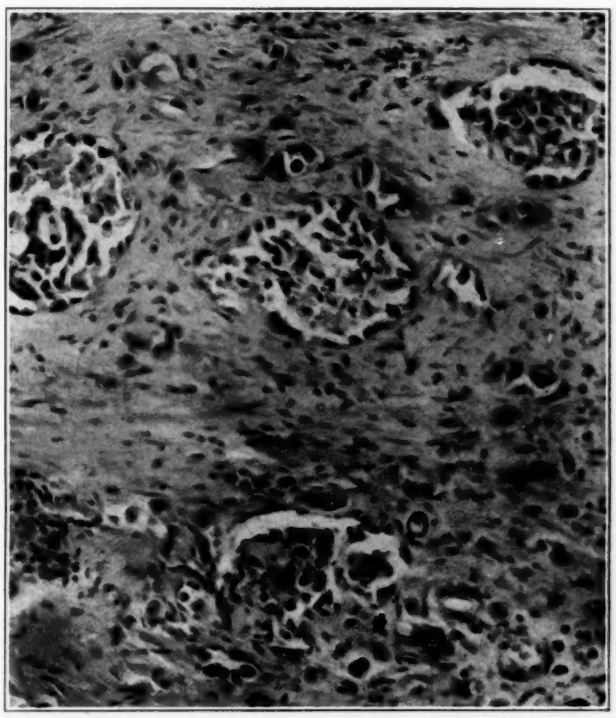

Fig. 6.—Section under higher power showing tumor cells between muscle bundles and connective tissue fibers as well as within endothelium-lined channels.

The patient had a bad night and complained of nausea and headache. Again the temperature was elevated and the pulse rate was accelerated. On the third day the output from the right kidney by catheter was 1,220 cc., and that from the left, over 540 cc. On that day the catheters again ceased functioning and were removed, fresh catheters being inserted in the afternoon. The urinary output continued as usual.

On the fourth day the blood pressure dropped to 128 systolic and 82 diastolic. The pulse rate was 130, the respiratory rate was 20, and the temperature averaged 102 F. No estimation of the amount of urine passed through the catheters was possible on account of the frequent irrigation, the amount of which was not checked. There seemed to be slight improvement in the patient's condition.

25. Schlagintweit, cited by Glas.[3]

On the fifth day the urinary output for the twenty-four hours was 1,600 cc. Chemical examination of the blood revealed 50 mg. of urea nitrogen, 1.58 mg. of creatinine and a carbon dioxide combining power of 48. Indigo carmine given intravenously appeared on the left side in four minutes, showing a 2+ concentration. On the right side it appeared in twenty minutes with a 1+ concentration. The patient continued to improve from the standpoint of chemical blood analyses, and the total urinary output averaged from 1,400 to 2,000 cc. in twenty-four hours, as long as the catheters remained in place.

Indigo carmine was injected intravenously on the sixth day and appeared in ten minutes with a 2+ concentration from each kidney. Urinary cultures showed B. coli from each kidney and a nonhemolytic streptococcus from the right kidney. Any attempt to remove the catheters was followed by total failure to pass urine into the bladder, a sharp rise in temperature, severe chills and a general breaking down of the patient's morale.

Despite the patient's poor condition it was decided to institute nephrostomy drainage of the right kidney. This was successfully accomplished on the ninth day without any apparent shock to the patient. At operation the upper portion of the ureter was noted to be much thickened, indurated and inelastic but

Fig. 7.—Low power view of periureteral tissues showing nests of tumor cells within the perivascular lymphatic channels. Note the occluded blood vessels with neoplastic tissue within its wall.

did not give the appearance of a malignant condition. The drainage from the nephrostomy was, however, somewhat disappointing, the amount being much less than had been obtained by catheter drainage. The course for the next three days was satisfactory, the temperature remaining around 100 F. and no chills intervening.

On the fourteenth day the twenty-four hour output was 900 cc. from the nephrostomy tube and 650 cc. from the catheter in the left kidney. The blood chemistry values, however, began to rise, showing 81 mg. of urea nitrogen, 3.52 mg. of creatinine and a carbon dioxide combining power of 44. Indigo carmine again appeared from each side in ten minutes and showed a 1+ concentration.

The patient's condition became progressively worse, although the urinary output was within fair limits, owing probably to the large amount of medication given intravenously, subcutaneously and through a duodenal tube. The plan to perform nephrostomy of the left kidney was abandoned because of the patient's poor condition. On the eighteenth day after admission the patient died.

Postmortem Examination.— In the anterior portion of the vagina, in the region of the fornix, there was found an area of ulceration which almost completely encircled the cervix. It extended externally on the left side for a distance of about 1 cm. and internally on the external os of the cervix. The uterus showed no significant changes on gross examination.

The ovaries were slightly enlarged. In them were seen a few grayish nodules, especially near the ligamentous attachment. The tubes were slightly thickened, but their lumens could be probed. On cut section the thickening was found to be due to grayish cellular tissue, subperitoneally located, which did not communicate with the lumen.

The urethra and trigon were injected.

There was a nephrostomy opening in the right kidney and evidences of a purulent perirenal inflammatory reaction extending to the upper portion of the ureter. The capsule of the right kidney could not be stripped. The cut surface of the kidneys had a grayish appearance, and scattered throughout, most pronounced in the lower portion, were numerous grayish necrotic areas ranging in size from that of a pinpoint to that of a pinhead. The lower half of the pelvis of the left kidney was necrotic and gangrenous. The remainder of the pelvis was thickened and had a granular surface. The right kidney also was slightly enlarged, but the small, necrotic areas were not as numerous as in the left kidney. The pelvis of the right kidney was markedly hemorrhagic.

The two ureters showed essentially the same changes. The walls of the upper portion of the ureters were thickened. At one point in the right ureter, about 2 cm. below the ureteropelvic junction, the wall was firm, inelastic, sclerosed and intimately adherent and fixed to the periureteral tissue. However, with moderate difficulty the lumen could be probed. The lower two thirds of the ureters also were slightly thickened and inelastic; the last 2 cm. showed no obvious gross change. The left ureter in its second upper centimeter was denuded of epithelium and instead there was an ulceration with necrotic tissue in the base. This was just above the point at which the ureter was fixed to the periureteral tissues. The ureters were not in direct contact with any of the tumor masses in the other organs. Both ovarian veins were surrounded by a type of tissue similar to that surrounding the upper portion of the ureters. This was most marked about the left ovarian vein, in which there was a thrombus extending for a distance of about 10 cm. up to its opening into the renal vein.

Microscopic examination of the tissue in the fornix showed an ulcer, in the base of which there were epidermoid cells infiltrating, in the form of pegs, into the deeper layers. There was moderate atypism and irregularity with not infrequent mitotic figures. Immediately beneath this the tumor cells were found to be within the perivascular lymphatic vessels. The deepest tissues of the cervix and vagina showed a minimal involvement by tumor tissue.

Both kidneys showed evidences of pyelonephritis.

The conditions of the two ureters were similar. There was a pronounced invasion of the outer layers of the muscularis and perimuscular region by tumor cells. Mitotic figures were frequent. There was a prominent scirrhous reaction about the nests of tumor tissue. These neoplastic cells were found to be present not only between the individual muscle fibers but also in the perivascular lymphatic channels in the periureteral tissue.

The nodules in the tube and ovary were found to be made up of tumor cells. Sections taken through the ovarian veins showed tumor tissue in the perivascular and perineural lymphatic vessels, as well as within the walls of the veins. These cells extended to the intima. Some of the smaller radicles were completely occluded by an organizing thrombus, in the meshes of which some tumor cells were found. The thrombus in the ovarian vein was found to be in apposition with that portion of the wall which was invaded by tumor tissue.

A lymph node removed from the region in which the involvement of the ureter, as well as of the ovarian vessel, was most pronounced, showed no invasion by tumor tissue.

COMMENT

As to the mechanism causing obstruction by tumor nodules within the ureter proper, one must consider various possibilities. Most frequently obstruction is due to an expansive growth of the nodules with encroachment on the lumen. I shall mention only those cases in which the tumor arises in adjacent tissue and

compresses the ureter from without. There are also cases in which a sclerosing reaction to the tumor cells results in stricturizing with obstruction. These, however, do not explain the case herewith described. On the left side the ureteral lumen was obstructed and the catheter was passed with difficulty. The predominant factor was the marked fibrosis in the ureteral wall with contracture of the connective tissue, thereby occluding and markedly narrowing the lumen. On the right side, however, the ureter was patent and yet no urine passed except through an indwelling catheter. The scirrhous infiltration of the wall with some narrowing of the lumen was an appreciable factor but could not entirely explain the failure of passage of urine, nor could the additional factors of lack of peristalsis and nervous involvement completely account for it. The possibility that edema had disappeared before necropsy is plausible and likely. One must, however, consider also invagination of the upper ureteral segment into the thickened and scirrhous portion, which is extensively and firmly fixed to the periureteral tissue. A wave of contraction in the superior portion, which is not so markedly infiltrated, reaches this fixed position and, not being able to pass along, invaginates the upper segment into the sclerosed fixed lower area. Telescoping with resultant intussusception, which is so frequently found in the intestine, cannot take place because of the rigidity of the lower tube and its lack of expansile power. However, the mere dimpling-in of the upper into the lower segment may be sufficient to act as an obstruction to the passage of urine.

ABSTRACT OF DISCUSSION

DR. H. S. JECK, New York: Dr. Woodruff's classification of metastatic tumors is admirable in its simplicity. His interesting case of bilateral metastatic carcinoma falls in the group of true metastases. I agree that one should not be too meticulous in including in this true metastatic group only those tumors that show cancer cells in the lymph channels and the blood stream. At autopsy many of these tumors are doubtless true metastases, but it is difficult to prove it. However, the pathologist who performs the autopsy is often convinced of the true metastatic character by the relationship of the gross conditions observed. With reference to the implantation of tumor cells in the ureter from papillary carcinoma of the kidney, it is doubtful that this ever occurs. It would imply a pathologic condition of the ureter of some sort, such as an obstructed ureter or an inflamed ureteral mucosa or a combination of the two. I recently operated on a patient who comes under Dr. Woodruff's group classification II. The upper end of the ureter was considerably dilated, there was an obstruction about 12 cm. down from the ureteropelvic junction and as far down as one could reach one could feel friable, firm tissue surrounding the ureter. Some of this tissue was removed and proved to be carcinomatous. I have a case which I believe belongs to the third group. The pathologist was of the opinion that it was a case of true metastasis. The history obtained, in this man of 60, indicated that six months prior to his admission he had had sharp, intermittent pains in the left loin, followed by polyuria. For a short period he had noticed blood in the stools. An attempt was made to catheterize the ureters but I couldn't find any ureteral orifices. Roentgenograms suggested stones in the region of both kidney pelves. Nephrostomy on one side was decided on and possibly bilateral nephrostomy, depending on the condition encountered at operation. During the incision for exploration of the left kidney, much fluid poured from the loin wound on account of the edema, and when the fascia transversalis was incised a big mass presented itself in the wound. This proved to be the kidney. An opening into the kidney pelvis directly through the parenchyma was made by means of a hemostat. Urine under considerable pressure gushed from the nephrostomy wound. The kidney pelvis was explored but no stone could be felt. A rubber tube was inserted in the kidney and the loin incision was closed and an incision made in the right loin. The patient was so edematous on this side that I cut down where I thought the kidney was. It happened to be a little below the kidney pelvis and a greatly distended ureter came into view, so I stuck a hole in this, sewed a catheter in the ureteral opening, and closed the loin incision. The patient lived only about twenty hours after the operation. Autopsy revealed an ulcerating carcinoma of the sigmoid with stenosis, with metastases to the peritoneum and retroperitoneal nodes to the liver and both ureters. Both ureters were completely occluded by the metastatic nodules. While comparatively few cases of bilateral metastatic malignant lesions of the ureters have been reported, attention has now been so focused on the condition that one should always bear it in mind as a possibility when bilateral ureteral obstruction is suspected.

DR. A. E. BOTHE, Philadelphia: A patient was first seen on account of hematuria; no other symptoms were associated. A pyelogram showed a filling defect. The kidney was removed, a tumor was found in the pelvis and a diagnosis of benign papilloma was made. About four years after removal of the kidney, hematuria occurred again. At that time I found a papillary tumor protruding from the ureteral orifice on the side on which the kidney had been removed. The patient was advised to have irradiation, and this was followed by ureterectomy. A photomicrograph showed that the tumor in this particular part was not infiltrating the wall of the ureter. This last removal was about a year and a half ago. He has had postoperative irradiation. Cystoscopy about a week ago gave no evidence of any tumor in the bladder and the patient is perfectly well.

DR. F. C. HERRICK, Cleveland: I readily appreciate involvement of the ureter from above down. The part of especial interest has been ascending growth in the periureteral lymphatics. It does not seem to me that there has been enough emphasis placed on this in the literature. I mentioned it twelve or fourteen years ago, since which time a pathologist called my attention to a prostatic carcinoma in which he had demonstrated metastatic growths in the ureteral wall and periureterally, extending up to approximately the upper third of the ureter, then leaving that point and going into the cortex of the kidney. That is along the line of the extension of infection as described by Schultz and Eisendrath. Since then I have seen perhaps four or five similar cases in the pathologic departments in Cleveland. The last two were carcinoma of the prostate and carcinoma of the cervix, respectively, in which periureteral, intramural ureteral extension of the growth was proved at autopsy with the growth implanted into the cortex of the kidney. That, to me, is very strong evidence of the ascending route. Along the line of infection transmission, in the past I had a patient with papillocarcinoma on the left side of the bladder, a small one, which I resected, following which it cleaned up very well. He was home a week when he had violent chills, high fever and a very tender, large left kidney. It was perfectly obvious that he had involvement of the left kidney. The local handling of the bladder had been resection, careful closure and drainage intracystically and in the deep pelvis on that side; the drain was removed in three or four days. There was no evidence of infection locally. He was taken back to the hospital and exposure of the left kidney was made. The fatty capsule in these cases is thick and edematous; it is a thick, firm, inflammatory type of fat. Multiple abscesses were evident in the cortex of the kidney. A quick nephrectomy was done, from which he recovered very nicely. All the infection and all the abscesses were cortical and just beneath the capsule of the kidney. That, together with the evidence from tumor metastasis, I cannot help but explain by ascending periureteral lymphatic extension.

DR. STANLEY R. WOODRUFF, Jersey City, N. J.: I brought up this subject mostly for the reason that it affords another thing to think about in acute anuria. It has been customary to think that anuria is caused always by calculous disease, or possibly, toxic nephritis. However, this condition must be thought of.

MALIGNANT HYPERPLASIA OF THE LYMPH FOLLICLES OF THE SPLEEN

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PITTSBURGH
AND
H. G. LITTLE, M.D.
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In 1925 Brill, Baehr and Rosenthal [1] reported three cases of what they called splenomegalia lymphatica hyperplastica. Their observations and review of the literature led them to believe that there had been reported previously only one other similar case, that of Becker in 1901. Several cases were noted of splenic lymph adenosis in which there was lymphoid hyperplasia confined to the spleen and in which splenectomy had been performed.

In 1927 Dr. R. D. Baker reported a case of splenomegaly with enlargement of the lymph nodes, notably the posterior auricular, occipital and inguinal. Biopsy showed giant lymph follicle hyperplasia. With roentgen treatment the glandular involvement receded, but the red blood cells and the bone marrow were damaged. The man died in 1930 and the case was finally diagnosed as chronic lymphatic leukemia.

It was our good fortune to study and treat a case in 1927 similar in most respects to the cases reported by Brill, Baehr and Rosenthal:

History.—Mrs. T. R., aged 28, reported for an examination in April 1927, because of a mass in the abdomen, which had been discovered by her family physician. For two months previously she had noticed a heaviness in the left side of the abdomen and an occasional shooting pain down toward the left pelvis. There had been a tendency to flatulence and constipation. She also had shortness of breath. She had been nursing continuously up until this time a 10 months old baby. Her weight was normal. The menses had been established three months after childbirth and were normal.

In childhood she had had diphtheria and scarlet fever, and in 1915 an uncomplicated and moderately severe attack of typhoid. She had been married for five years and had two children, aged 3 years and 10 months, respectively.

The family history was essentially negative.

Examination.—The patient was well nourished and slightly pale. She weighed 115 pounds (52 Kg.). The teeth were in good condition, the thyroid was small and the tonsils were submerged and normal. The eyes and ears were normal, the tongue was clean, and superficial lymph nodes were not palpable. The heart was normal, except for a soft systolic blow in the pulmonic area. The pulse was regular, with a rate of 80. The blood pressure was 110 systolic, 70 diastolic. The vessel walls were not palpable. The lungs were normal.

The abdomen was asymmetrical owing to the presence of a smooth mass in the left flank, which had the characteristic contour of the spleen extending from the eighth left intercostal space above to the crest of the ilium below. It was slightly tender and slightly movable, especially from side to side. The right kidney was normal in size, palpable and movable to the second degree. The left kidney was not palpable. The liver was of normal size. There was no free fluid demonstrable.

Examination of the blood, April 4, showed: hemoglobin, 88 per cent; red cells, 4,100,000; white blood cells, 4,500; polymorphonuclear leukocytes, 60 per cent; small mononuclears, 25 per cent; large mononuclears, 15 per cent; blood platelets, 197,000; bleeding time, two minutes; coagulation time, six and one-half minutes. The Wassermann reaction was negative. The blood sugar was 90 mg. per hundred cubic centimeters and the nonprotein nitrogen, 29 mg.

Urinalysis showed a cloud of albumin with a small number of granular casts, a few red and white cells and débris. This was confirmed in several examinations. Stool examination was negative for blood and ova.

The bladder was normal; a number 5 catheter was passed to both kidneys. Indigo carmine given intravenously appeared on the right side in two minutes, and on the left in three minutes. The urine from the right kidney was normal. Urine from the left kidney contained red blood cells and granular casts. A pyelogram showed both kidney pelves normal. There was a prolapse of the right kidney.

Roentgen study of the gastro-intestinal tract showed that the stomach was atonic, prolapsed and dilated, with a slight six-hour residue. The meal reached the rectum in twenty-four hours. The splenic flexure of the colon was prolapsed. The mass apparently had no connection with the stomach.

The urinary changes pointed to a lesion of the left kidney, suggesting the possibility of the tumor being an enlarged kidney. The physical and roentgen examinations, however, were quite conclusive of an enlarged spleen. It was impossible from the history and the physical examination to determine its etiology. An exploratory operation was advised and accepted.

Malignant hyperplasia of the lymph follicles of the spleen under low power.

Operation.—April 13, with nitrous oxide anesthesia and local procaine hydrochloride infiltration of the abdominal wall, an exposure through the left rectus muscle was made. The tumor was a spleen, weighing 3½ pounds (1,587 Gm.). The external contour, color and consistency were normal. The peritoneal surface was smooth but marked by innumerable, small yellowish white depressions. No peritoneal adhesions were found. There were three arteries and veins in the pedicle. Removal offered no technical difficulties.

The liver was a reddish brown. It was normal in size and appearance. The gallbladder was normal. There were two enlarged lymph glands in the gastrosplenic omentum. The larger, measuring 2 cm. in its longest diameter, was removed for examination. No other enlarged lymph glands were seen anywhere. The pancreas was normal. The stomach was outwardly normal and not prolapsed. The small intestine and colon were normal. The appendix was atrophic and nonadherent. The kidneys were normal in size. The right kidney was freely movable. The pelvic viscera were normal.

Postoperative Course.—Convalescence was entirely normal and uneventful. The abdominal wound healed by primary intention. The patient left the hospital, May 3, feeling well. Her weight was 110 pounds (50 Kg.). Examination of the blood on that date showed: hemoglobin, 98 per cent; red blood cells, 4,400,000; white blood cells, 11,100; polymorphonuclear leukocytes, 79 per cent; small mononuclears, 15 per cent; large

1. Brill, N. E.; Baehr, George, and Rosenthal, Nathan: Generalized Giant Lymph Follicle Hyperplasia of the Lymph Nodes and Spleen, J. A. M. A. 84: 669 (Feb. 28) 1925.

mononuclears, 6 per cent; blood platelets, 222,000. The bleeding time was two minutes. Coagulation time was three and one-half minutes. Urinalysis subsequent to the operation was normal.

Since leaving the hospital, the patient has been enjoying excellent health. She gave birth to a third child, Sept. 18, 1929. There was no development of enlarged lymph nodes. She now weighs 130 pounds (59 Kg.).

Pathologic Examination (By Dr. H. G. Little).—The spleen, weighing 3½ pounds, measured 22.5 by 11.3 by 6.5 cm. It was a dark reddish brown, markedly increased in size, and firm; the capsule was smooth, save for a small area of perisplenitis. The surface was a reddish brown and the pulp moderately firm. Scattered throughout the surface were many small grayish nodules resembling miliary tubercles. There were no infarcts in the spleen. The sections showed without the microscope they alone are involved in the disease process. It is, we feel, of malignant character and at the present time is classified as malignant hyperplasia. It is interesting to note that the patient has had three infectious diseases which usually involve the spleen. The inflammatory reaction seen in the sections may be induced by the tumor growth, as sometimes seen in a lymphoblastoma or by some infection. The prognosis would seem to be poor, because of involvement of a neighboring lymph node; yet tumors of lymphatic tissue respond splendidly at times to x-rays alone or to surgery and x-rays.

Sections of the tumor were sent to Dr. G. R. Callender, Lieutenant Colonel, M. C., U. S. Army, at the Army Medical Museum, for the lymphatic tumor

TABLE 1.—*Protocols of Cases of Malignant Hyperplasia of the Lymph Follicles of the Spleen*

	Case 1 (Dr. Baehr)	Case 2 (Dr. Baehr)	Case 3 (Dr. Baehr)	Case 4 (Herein Reported)
Age	28 years	32 years	.....	28 years
Sex	Female	Female	Female	Female
Family history	Negative	Negative	Negative	Negative
Past history	Negative	Influenza 1 year before	Negative	Diphtheria, typhoid, scarlet fever
Onset	Glandular swelling of neck for 2½ months; dyspnea, cough, increase in size of abdomen	Weakness, increase in size of abdomen, and for 2 months heaviness	.....	Heaviness for 2 months; flatulence, constipation, dyspnea
Physical examination.	Left pleural effusion			
Lymph nodes	All enlarged, especially cervical—size of pea to walnut; discrete, not tender, movable	Axillary, epitrochlear; left inguinal moderately enlarged	General enlargement	Not enlarged
Spleen	Eighth left rib to anterior superior spine of ilium and 5 cm. to right of midline; smooth, not tender	Eighth left costal space to brim of pelvis and within 2 cm. of midline; smooth, nontender	Large	From eighth left costal space to crest of ilium; slightly tender and movable
Liver	Not enlarged	Greatly enlarged	.....	Not enlarged
Blood:				
Hemoglobin	72%	95%	75%	88%
Red blood cells	4,700,000	4,900,000	3,200,000	4,100,000
White blood cells	6,000	11,000	6,000	4,500
Platelets	160,000	105,000	.....	197,000
Polymorphonuclear leukocytes	71%	42.3%	48%	60%
Large lymphocytes	15%	49.3%	46%	25%
Large mononuclear leukocytes	10	7	3	15
Eosinophils	3	1	2	..
Basophils	0	0.3	1	..
Treatment	Roentgen therapy: x-rays	Splenectomy: x-rays	Splenectomy	Splenectomy
Result	Spleen regained normal size; lymph node diminished; finally disappeared by second course of irradiation; patient well September 24, 1½ years after treatment; died February 1930 with mediastinal infiltration	Followed by lobar pneumonia; subphrenic abscess; typhoid; enlarged lymph nodes disappeared in 3 months; recurred and disappeared with x-rays; patient well January 1925, 20 months after splenectomy	Died after splenectomy	Removal of two glands in gastrocomentum; no further lymph node enlargement; patient well July 1935
Pathologic changes	Spleen: huge malpighian bodies roughly size of barley grain; follicles greatly enlarged; little intervening pulp; lymph sinuses obliterated by compression; cells endothelioid, looking like lymphoblasts; lymph nodes corresponded grossly and microscopically to splenic changes	.....	.....	Spleen; weight 3½ pounds; innumerable grayish nodules resembling miliary tubercles (microscopically); follicular hyperplasia; lymph node corresponded grossly and microscopically to splenic changes

large hyperplastic follicles. With it, the increase in the size of the follicles was seen to be due to a fairly compact cellular growth of the cells in the germinal centers. The cytoplasm of the cells was pale staining and delicate. The nuclei showed a moderate amount of chromatin and some nuclei were clear except for one or possibly two large well defined nucleoli. This cellular hyperplasia was taking place in every follicle in the section, and in some areas new foci appeared to be developing. Although the follicles dominated the picture, there was an associated hyperplasia of the lymphoid cells in the reticulum. Occasional mitotic figures were seen. A moderate number of polymorphonuclear leukocytes and an occasional eosinophil were found. There was no evidence of tuberculosis in the sections. The section of the lymph node showed a picture similar to that in the spleen.

The growth was different from the sarcomatous type of lymphoblastoma. Although the extremely large follicles dominated the picture, we do not believe that

registry. He commented that in 1929 it was the only case in the registry that showed a similar picture in both spleen and lymph nodes and that because of this dual involvement the prognosis was very poor. He wrote further: "The classification of such a case was very difficult, and I think hyperplasia, to distinguish it from definite sarcomatous reaction, is justified at present."

In a recent communication he [2] writes:

> Your case has been classified under the nodular type of leukemic lymphocytoma described originally by Symmers as giant follicular hyperplasia with splenomegaly. There are twenty-three cases in the registry now with this diagnosis; fourteen are living; eight are dead; and one has been lost track of.

2. Callender, G. R.: Personal communication to the authors from Fort Sam Houston, Texas.

Dr. Baehr,[3] in referring to this disease, has commented as follows:

The tumor differs from ordinary lymphosarcoma in that it produces follicles and is multicentric in origin. The clinical picture is also quite different from lymphosarcoma, unilateral exophthalmos due to orbital infiltrations occurring commonly, as well as scattered involvement of the lymph node and lymphatic tissue in various parts of the body. There is no tendency to anemia or cachexia. The importance of differentiating these cases clinically and pathologically from ordinary lymphosarcoma is the fact that they respond so promptly and effectively to radiotherapy. I have seen mediastinal infiltration, which is large enough to choke the patient almost to death, begin to disappear after a few exposures to one fifth of an erythema dose. The oldest case under observation at present has lasted over ten years. Another case which I reported in 1925 died this morning, Feb. 14, 1930, as a result of mediastinal infiltration which had been neglected. The large splenomegaly, which in 1924 had disappeared completely under x-ray therapy, reappeared for the first time several weeks ago. The hydrothorax, which had brought the patient to me in 1923, also had reappeared. There seemed to have been a fulminating relapse, and death occurred before the radiotherapy could accomplish much. The prognosis is far better than with other malignant neoplasms because of the remarkable radiosensitivity. The patient should be constantly under observation so that the first recurrence of lymph node enlargement anywhere in the body should be promptly treated.

Protocols of the cases referred to by Dr. Baehr are given in the accompanying table.

With present knowledge it may be said that the etiology of this hyperplasia of the lymph follicles of the spleen is unknown. It seems very definitely to be a neoplastic process, although its kinship to lymphosarcoma, as Dr. Baehr says, is far from established.

The symptomatology is concerned with the enlargement of the spleen. If there is mediastinal glandular involvement, or pleural effusion, there may be dyspnea and cough. Enlargement of the spleen comes gradually over several months and causes a heavy feeling but not characteristically any pain. There is no loss of weight and no cachexia. There is apt to be secondary anemia but nothing characteristic in the blood picture.

The diagnosis will be established with certainty only by pathologic examination of the lymph glands or the spleen. It will not be confused with the splenic enlargements of the blood dyscrasias such as leukemia, hemolytic icterus, purpura haemorrhagica and polycythemia vera, in which the blood picture and reactions are characteristic; nor will the enlargements of the specific infections such as syphilis, tuberculosis, typhoid, and malaria be hard to distinguish. The splenomegaly of the so-called splenic anemia will be more difficult to differentiate, particularly in the early stages before gastric hemorrhage and enlargement of the liver or severe anemia develop. The splenic enlargement of Gaucher's disease may likewise cause difficulty. Tumors of the spleen such as benign lymphomas and lymphosarcomas will defy differentiation clinically at the outset.

Individuals with this disease untreated either die rather quickly or, if life is prolonged, develop ultimately fatal sarcomatous changes in the lymph glands and spleen with metastasis. With treatment, life may be prolonged many years; if undertaken early enough and adequately, a cure of the disease may be effected.

TREATMENT

Two courses of treatment are open: roentgen therapy and splenectomy. Both have been successful. Apparently roentgen irradiation will restore the spleen to normal size and cause lymph node enlargement to disappear. There are no data to show that this primary effect is permanent. On the contrary, it would seem that there is need of repeating at intervals a course of irradiation to the spleen and various groups of lymph glands. Particularly must the mediastinal nodes be watched.

In our case, splenectomy alone served to effect a cure; that is, the patient is living and well at the end of nearly eight years. It was striking in this case that there was no enlargement of the lymph nodes on the exterior of the body, and that intra-abdominally only several immediately adjacent to the spleen were found. This suggests that metastasis to the lymph nodes takes place slowly and only after the primary splenic hyperplasia is well developed. Possibly successful treatment in this case is linked definitely with the fact that at the time of the splenectomy there had not been metastasis or development of the process in the peripheral nodes.

Provided there was no specific contraindication to operation, in another case we should be tempted to do a splenectomy first and then treat the lymphatic system by irradiation as need be. In absence of lymphatic enlargement suitable for biopsy, it will be necessary to examine the spleen itself to establish the diagnosis. Irradiation should be deferred until this is done.

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3. Baehr: Personal communication to the authors.

THE TREATMENT OF MILK ALLERGY AND ITS BASIC PRINCIPLES

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Hypersensitiveness to milk presents a problem of general interest, although it may be of more immediate concern to the pediatrician. Its manifestations are many and include conditions varying from the mildest to the most severe forms of gastro-intestinal disturbances, eczema, urticaria, asthma, mucous colitis, migraine, acne, marasmus and pylorospasm. The foreign literature particularly has been replete with studies by such eminent pediatricians as Schlossmann, Finkelstein, Hutinel, Finizio, Barbier and Weill-Hallé, who have stressed the importance of the consideration of milk allergy in the field of infant feeding and who have cited cases which have eventuated either in most severe shock reactions or even acute anaphylactic death from the ingestion of milk. Moro [1] and Bauer [2] first described cases of marasmus due to milk intolerance and showed that this condition could largely be attributed to immunologic disturbances resulting from the entrance of the milk proteins into the blood stream. Schloss and Worthen, and Anderson and Schloss [3] in America amplified this concept. More recently, in the French monograph of Laroche, Richet and St. Girons and in the excellent and more complete textbook on food allergy by Rowe [4] of California, emphasis was

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1. Moro, E.: Kuhmilchpräzipitin im Blute eines 4½ Monate alten Atrophikers, München. med. Wchnschr. **53**: 214, 1906.
2. Bauer, J.: Ueber den Nachweis der precipitablen Substanz der Kuhmilch im Blute atrophischer Säuglinge, Berl. klin. Wchnschr. **43**: 711, 1906.
3. Anderson, A. F., and Schloss, O. M.: Allergy to Cow's Milk in Infants with Nutritional Disorders, Am. J. Dis. Child. **26**: 451 (Nov.) 1923.
4. Rowe, A. H.: Food Allergy, Philadelphia, Lea & Febiger, 1931.

laid on the fact that allergy to milk is encountered more frequently than most physicians are aware of, not only in early infancy but well on into adult life. Space does not permit a fuller presentation of the clearly proved evidences of idiosyncrasy to milk, but suffice it to say that the insidious influence that the ingestion of raw milk proteins must have in human afflictions is great indeed and not often enough recognized or adequately understood.

PATHOGENESIS

Many theories have been advanced to account for the development of allergy, and it would necessitate a wide digression to consider all the factors that have been proposed in explanation. There are in the main two schools of thought, one proposing that it is inherited, the other that it is acquired. My own experience leads me to stand with the latter school. The following discussion of the pathogenesis evolves from factual evidence gathered from clinical observation and laboratory experimentation.

A. *Congenital Sensitization.*—1. Passive Sensitization in Utero: It has been demonstrated by Rosenau and Anderson, Wells and many others [5] that a fetus can be passively sensitized in utero. In relation to the human infant, such passive sensitization would occur only when the mother was sensitive to milk, the fetus being sensitized by the transfer of milk antibodies through the placenta. This phase I believe plays a minor rôle.

2. Active Sensitization in Utero: With the cooperation of Professor Jackson and Miss Gruehl I [6] published a series of studies showing that a guinea-pig fetus can be actively sensitized in utero, by which I mean that the specific antigen is transferred from the pregnant female to the fetus through the permeable placenta, and antibodies to this antigen develop after birth. This observation laid the groundwork for a clinical study in which I [7] postulated that a pregnant woman indulging excessively in protein foods during the latter months of pregnancy could actively sensitize the human fetus to the particular food, or foods, consumed to excess. Up to that time there had been no valid explanation for those instances in which infants manifested allergic reactions on taking milk or other protein foods for the first time.

B. *Sensitization Through the Gastro-Intestinal Tract.*—Rosenau and Anderson, Richet, Ascoli, Wells and others [8] showed that proteins administered orally can pass directly through the intact intestinal wall and enter the blood stream. Walzer [9] demonstrated this in the human adult with fish and egg proteins, and Anderson, Schloss and Myers [10] in the normal infant with milk, egg and almond. More recently Ratner and Gruehl [8] showed that milk proteins fed to guinea-pigs entered the blood stream with such frequency that they contended that such a passage is a normal phenomenon. Duke and Stofer [11] cited the remarkable case of a donor who drank a considerable amount of milk before his blood was used for a transfusion. The recipient, a woman aged 63 who was allergic to milk, had a violent allergic reaction that may be attributed to the milk proteins circulating in the donor's blood.

In our study we [8] have indicated that although the intestinal wall is normally permeable to proteins, abnormal conditions may increase its permeability and may account for sensitization in the following circumstances:

3. An occasional feeding of raw milk during the new-born period, when the intestinal wall is naturally more permeable, may give rise to a state of hypersensitiveness which is manifested when the child is later given raw cow's milk either to supplement breast feeding or when it is weaned from the breast.

4. Periods of excessive ingestion of raw cow's milk followed by periods of complete abstinence may also result in sensitization.

5. In persons who are fed raw milk during convalescence from some disease or during and after severe gastro-intestinal disturbances, hypersensitiveness may develop.

C. *Sensitization from Parenteral Injections of Milk.*—This is illustrated by the case reported by Lubiner,[12] who described a nearly fatal reaction following the intramuscular injection of 10 cc. of milk into a girl eight days after the last of three daily injections. Many other cases have been reported.

IMMUNOCHEMISTRY OF MILK PROTEINS

According to Wells and Osborne [13] milk contains four distinct proteins, or protein fractions; namely, casein, lactalbumin, lactoglobulin and an alcohol-soluble protein. By immunologic means, particularly the anaphylactic test, it has been shown that these four proteins are immunologically distinct. Of the four proteins only globulin is related to the beef serum, but the lactalbumin and the serum albumin are two distinct proteins. Biologically casein is as distinct from the whey proteins and serum proteins as it is chemically, whereas the biologic reactions of caseins from the different species of animals show close relationships. The albumins, however, differ immunologically in the various animal species. To recapitulate, therefore, casein represents a protein that is common antigenically in the milks of various animal species; lactoglobulin is a counterpart of the serum globulin from the same animal and is species specific, and lactalbumin stands alone as an independent protein, foreign to the blood stream and not related to the casein and is species specific.

One of the fundamental principles relative to the chemistry of proteins is that a protein cannot induce sensitivity or shock reactions in a sensitized human being or animal unless it is at once readily soluble and in a native or unchanged state. It must be soluble in order to pass through living membranes and enter the blood circulation to reach sensitized smooth muscles in the various organs; and it must be native or unchanged because the higher degradation products of the proteins, which result from proteolytic digestion, namely, the polypeptides, proteoses and peptones, and the completely hydrolyzed constituent amino acids, have all been shown to be incapable of serving as sensitizing or shock-producing substances. When milk enters the digestive tract, it undergoes a precipitation or curd formation

5. Ratner, Bret; Jackson, H. C., and Gruehl, Helen L.: Transmission of Protein Hypersensitiveness from Mother to Offspring: I. Critique of Placental Permeability: IV. Passive Sensitization in Utero, J. Immunol. **14**: 249 and 291 (Nov.) 1927.

6. Ratner, Bret; Jackson, H. C., and Gruehl, Helen L.: Transmission of Protein Hypersensitiveness from Mother to Offspring: V. Active Sensitization in Utero, J. Immunol. **14**: 303 (Nov.) 1927.

7. Ratner, Bret: A Possible Causal Factor of Food Allergy in Certain Infants, Am. J. Dis. Child. **36**: 277 (Aug.) 1928.

8. Ratner, Bret, and Gruehl, Helen L.: Passage of Native Proteins Through the Normal Gastro-Intestinal Wall, J. Clin. Investigation **13**: 517 (July) 1934.

9. Walzer, Matthew: Studies in Absorption of Undigested Proteins in Human Beings, J. Immunol **14**: 143 (Sept.) 1927.

10. Anderson, A. F.; Schloss, O. M., and Myers, C.: The Intestinal Absorption of Antigenic Protein by Normal Infants, Proc. Soc. Exper. Biol. & Med. **23**: 180, 1925.

11. Duke, W. W., and Stofer, D. D.: M. Clin. North America **7**: 1255 (Jan.) 1924.

12. Lubiner: Deutsche med. Wchnschr. **44**: 547, 1918.

13. Wells, H. G., and Osborne, T. B.: Anaphylaxis Reactions with Purified Proteins from Milk, J. Infect. Dis. **29**: 200 (Aug.) 1921.

of the casein fraction which results from contact with the rennin and hydrochloric acid present in the stomach. The whey substances—containing the lactalbumin and lactoglobulin fractions with the carbohydrate and mineral constituents—pass unchanged through the pylorus and enter the small intestine. The precipitated casein then gradually leaves the stomach and enters the small intestine, where the digestive enzymes further act on it; there is small likelihood that this precipitated protein is in a sufficiently soluble state to escape through the intestinal wall into the blood stream before it is partially or even completely digested. This is not so with the whey proteins, which are still in a liquid state and highly soluble; it is conceivable that they may escape digestion and thus enter the blood stream before digestion alters their nativity and serve as anaphylactogens.

Other factors that may change the antigenic properties of the milk proteins will now be considered.

A. *Heated Milks.*—Wells [14] observed that casein heated to 100 C. for twenty-five minutes did not lose any of its anaphylactogenic properties. Cutler,[15] using the precipitin and complement fixation methods and anaphylactic test, more recently concluded from a study of raw, pasteurized and evaporated milks that in evaporated milk there is a 50 per cent reduction of the whey protein, and that there is a chemical change in specificity of these proteins. Lewis and Hayden [16] included smaco 303 in their study and employed the complement fixation test. All these investigators agreed that heat does not change the antigenic properties of casein, although Lewis and Hayden found that it begins to show a slight change when the heat reaches 100 C. All these investigators were in agreement on the fact that the whey proteins are specifically changed chemically by the process of heat and evaporation, and the latter indicated that the change occurs when the heat reaches 60 C.

I believe that these investigators have erred in concluding that a chemical change of specificity occurs as a result of the application of heat, which position we [17] have discussed in a recent paper on our study of the influence of the various heat processes on the anaphylactogenic properties of milk. We worked with purified proteins, whereas Cutler, Lewis and Hayden merely crudely separated the whey from the casein fraction. We have shown that unless the milk proteins are most exactingly purified they are always contaminated one with another. All the so-called pure caseins that we obtained from reliable sources gave marked reactions when tested against lactalbumin.

Casein is unaffected by the evaporation process and other forms of prolonged application of heat. We found no specific chemical change in any of the protein fractions as a result of the influence of heat; we sensitized animals with milk boiled for several hours, evaporated and superheated milks and shocked them with pure lactalbumin obtained from raw milk. But when we sensitized animals to pure lactalbumin from raw milk, we were unable to shock them with heated milks. We therefore concluded that the only change which occurs in the heated milks is a physical one, namely, coagulation of the whey proteins, which markedly diminishes the ability of the milks to induce anaphylactic or allergic reactions in human beings or animals sensitized to lactalbumin and lactoglobulin. In those of our experiments in which the antigen was administered orally to animals the diminution of the properties of sensitization and shock of heated milks was strikingly demonstrated.

B. *Dried Milks.*—We studied the antigenic changes that result from varying drying processes applied to milks and found that the rapid drying—which is almost instantaneous—did not influence or diminish the antigenic powers of the milk proteins. It is interesting to note that Hart, Steenbock and Ellis [18] showed that vitamin C still remains potent in dried milks. This vitamin is destroyed in evaporated or superheated milks. Since the milk in the drying process is not subjected to heat for a long enough period to affect the highly heat-labile vitamin C, our contention that the drying process does not influence the antigenic powers of the proteins is further supported. Chick and Martin [19] also showed that in order for coagulation to take place the proteins must be in a liquid state and that proteins that are dry resist the influence of heat.

C. *Acidified Milks.*—We found that acidification of milk in no way diminished the anaphylactogenic properties and as a matter of fact enhanced them. In our feeding experiments we succeeded most easily in sensitizing the largest percentage of animals with acidified raw milk. An explanation may be that just as in digestion the formation of the curd liberates the whey proteins and makes them more accessible for absorption into the blood stream. This is borne out by the fact that the lactalbumin as it exists in fresh raw milk is in such a condition that only a part passes through a porcelain filter; however, when the milk is acidified the lactalbumin is completely filtrable through the porcelain filter.

Before proceeding to a consideration of the treatment it may be helpful to evaluate the relative importance of the individual milk proteins as causative agents in milk allergy. From Hutinel, Barbier, Weill-Hallé and others it is learned that practically every patient with an idiosyncrasy to milk, no matter how severe, can be relieved from further allergic manifestations when taken off cow's milk and given goat's, ass's or human milk. In view of the independence of the lactalbumin and lactoglobulin fractions of the milks of the various animal species and the close relation of the casein fractions, one is forced to the conclusion that most of these persons, if not all, are sensitive to the whey proteins and not to the casein fraction. In those cases that are reported in the literature in which positive reactions to casein are shown one is faced with the difficulty, into which we have gone at such length, that the investigator may not have been using a truly purified casein; in this category must be placed such a publication as that of Anderson, Schloss and Stuart.[20] It must again be emphasized that the casein fraction is curded by contact with the gastric juices and thus impeded from entering the intestinal tract in a soluble form. This is

14. Wells, H. G.: Studies on the Chemistry of Anaphylaxis, J. Infect. Dis. **9**: 147, 1911.
15. Cutler, O. I.: Antigenic Properties of Evaporated Milk, J. A. M. A. **92**: 964 (March 23) 1929.
16. Lewis, J. H., and Hayden, H. C.: Effect of Heat on the Antigenic Properties of Milk, Am. J. Dis. Child. **44**: 1211 (Dec.) 1932.
17. Ratner, Bret, and Gruehl, Helen L.: Anaphylactogenic Properties of Milk: Immunochemistry of the Purified Proteins and Antigenic Changes Resulting from Heat and Acidification, Am. J. Dis. Child. **49**: 287 (Feb.) 1935.
18. Hart, E. B.; Steenbock, Harry, and Ellis, N. R.: J. Biol. Chem. **42**: 383 (July) 1920.
19. Chick, Harriet, and Martin, C. J.: On the "Heat Coagulation" of Proteins, J. Physiol. **40**: 404, 1910.
20. Anderson, A. F.; Schloss, O. M., and Stuart, H. C.: The Biologic Relationship Between Cow's, Goat's and Human Caseins, Am. J. Dis. Child. **44**: 1178 (Dec.) 1932.

not true of the whey proteins. From such reasoning it should follow that persons are more readily sensitized to the latter proteins. An interesting speculation is that in infants who have been breast fed a tolerance for the casein fraction develops which is antigenically related both in human and in cow's milk. From this brief summary it becomes apparent then that the treatment of intolerance for milk must be focused on the sensitivity to the soluble whey fractions. The points made here are interestingly illustrated in the following case. We believe that this case is unique in that purified proteins were used for testing purposes.

REPORT OF CASE

A boy, who was 9 years old when I first saw him, had been sensitive to cow's milk from early infancy. He was breast fed for eighteen months because when first given cow's milk he had a severe allergic reaction with vomiting and urticaria. When milk was subsequently given, he had severe attacks of asthma, even after taking only a few drops. The physician who studied this case for several years attempted to build up a tolerance for milk by giving drop doses, yet when the child was finally given one teaspoonful of milk he had a severe asthmatic attack with cyanosis; milk that was used in the preparation of foods provoked a reaction. The child was brought to me two years ago and the father was so insistent that milk was toxic for the child that he would not permit me to make a clinical trial with even a drop of milk. Tested by the scratch method, the child showed a moderate reaction to lactalbumin and to whole cow's milk. He was tested intracutaneously with the purified lactalbumin and casein (used in our experiments) in doses of 0.02 cc. of a 1 per cent solution of lactalbumin and with a similar dose (0.02 cc. of a 2.8 per cent solution) of casein. There was absolutely no reaction to the casein, but within a few minutes after the test with lactalbumin there developed a severe asthmatic attack with marked cyanosis and moderate dilatation of the right heart, and the child appeared to be going into anaphylactic shock. Restorative measures were applied, and epinephrine and oxygen administered. The boy remained in shock for several hours. The asthmatic phase continued for four days.

Serum taken from this patient and transferred to five guinea-pigs induced passive anaphylaxis in two of the animals. His serum was also transferred by the Prausnitz-Küstner method to the skin of several normal children and the presence of lactalbumin antibodies was demonstrated. One normal girl of 12 years, whose skin was locally sensitized, abstained from milk for forty-eight hours and was then given a glass to drink; a strongly positive local cutaneous reaction developed twenty minutes after ingestion. All these cases of passive local transfers were shown to be due to lactalbumin antibodies in the blood and not to casein. It may be noted that although raw milk in the smallest quantity provoked asthmatic attacks, and a minute amount of lactalbumin injected intracutaneously induced anaphylactic shock, this child was able to take reheated evaporated milk in normal amounts without the slightest reaction.

BASIC TREATMENT

In a case of milk allergy the first necessity is to eliminate all forms of whey proteins including raw milk as a beverage, milk used in the preparation of foods such as bread, cake, cream sauces, desserts, ice cream and cream of rice, and butter, dried milks, acidified raw milks, rare beef and beef serum.

The next problem is the substitution of some other form of milk. It has been stated that neither dry, acidified nor pasteurized milk nor milk boiled for a few minutes is of any true value in the treatment of patients with milk allergy. There is no uniform and perfectly standardized nonallergic milk. The only form that is valuable for substitution at the present time is that suggested by Kerley, who stated that milk boiled for from three to six hours is well tolerated. However, this is an irksome procedure and the commercial equivalent —evaporated milk—can readily and reasonably be purchased. However, it must be warned that evaporated milks are not standardized and that not all kinds are subjected to an adequate amount of heat. When evaporated milk is used in a severe case of milk allergy, it should be boiled vigorously for several minutes just prior to use. It is rather interesting at this point to note that Marriott, who originally advocated the use of acidified whole raw milk in infancy—which we have shown to be highly anaphylactogenic—later advocated the use of acidified evaporated milk. Denatured heated milk may be given to the milk intolerant infant in amounts adequate for nutrition, and to it may be added the proper carbohydrate requirement in the form of dextrimaltose or corn syrup, which we [21] have shown are nonanaphylactogenic.

In the early investigations goat's, ass's or human milk was suggested as a substitute for cow's milk, but these are not necessary if evaporated milk is used. It has also been recommended that the child who is acutely sensitive to milk should be given no milk, but broths, cereals and vegetables. More recently Hill and Stuart [22] advocated the substitution of a soy bean preparation. It is evident from this work and that of Tso [23] that soy bean can replace milk and that it fulfils the nutritional requirements of the child. However, while relief is obtained by such substitution, a tolerance for milk proteins is not built up. The child remains just as sensitive to the milk during and after the period of substitution by these foods as he was before their use. Since milk enters so largely into the diet of the adult as well as the child, I believe that an attempt should be made to build up a tolerance to milk proteins and that there should be no delay in attempting the ultimate cure of the intolerance for milk.

In view of the fact that we have shown that thoroughly heated milks are merely changed physically and that the chemical structure of the whey proteins still remain unchanged, such heated milks may be used indefinitely provided an adequate amount of vitamin C—which is the only factor destroyed—is added to the diet. It is believed by many pediatricians, among them Kerley and Brennemann, that heated milks have greater nutritive value because they are more readily digested and assimilated. With the use of heated milk and the complete elimination of all milk-containing foods one is ready to proceed with immunization by giving drop doses—or even a fraction of a drop—of raw cow's milk each day orally as Schloss,[24] Park [25] and I [26] have advocated. The quantity is very slowly and gradually increased, depending on the tolerance of the patient, and after a period of from six to nine months a normal amount of raw milk can generally be taken. From then on, as has been emphasized by French investigators, milk must be given continuously throughout the rest of the person's life in moderate amounts, either as a beverage or in foods.

21. Ratner, Bret, and Gruehl, Helen L.: Anaphylactogenic Properties of Malted Sugars and Corn Syrup, Am. J. Dis. Child. **49**: 307 (Feb.) 1935.
22. Hill, L. W., and Stuart, H. C.: Soy Bean Food Preparation for Feeding Infants with Milk Idiosyncrasy, J. A. M. A. **93**: 985 (Sept. 28) 1929.
23. Tso, Ernest: A Comparison of the Nutritive Properties of Soy-Bean "Milk" and Cow's Milk, Chinese J. Physiol. **3**: 353 (Oct.) 1929.
24. Schloss, O. M.: Allergy in Infants and Children, Am. J. Dis. Child. **19**: 433 (June) 1920.
25. Park, E. A.: A Case of Hypersensitiveness to Cow's Milk, Am. J. Dis. Child. **19**: 46 (Jan.) 1920.
26. Ratner, Bret: Eczema in Infancy Due to Protein Sensitization, M. Clin. North America **9**: 817 (Nov.) 1925.

Summarizing, the treatment of milk allergy consists in:

1. The elimination of all raw milk from the diet, including milk used in the preparation of foods.
2. The substitution of a milk subjected to intense and prolonged heat in a liquid state.
3. The gradual immunization of the patient by the oral administration of minute amounts of raw milk, with the continued use of the denatured milk throughout the entire period.
4. The final substitution of adequate amounts of raw milk, which must be taken from then on continuously in moderate amounts.

THE PREVENTION OF MILK ALLERGY

As important as it is to understand and treat patients with milk allergy properly, it is even more important to attempt to prevent the onset of the condition. I believe that this can be accomplished:

1. By advocating the taking of moderate amounts of milk during the period of pregnancy and the careful curbing of excessive indulgence in raw milk during the latter months of gestation so as to avoid the possibility of inducing congenital sensitization. If milk is desired in more than moderate amounts, part of the consumption should be in the form of denatured milk.
2. By avoiding isolated feedings of raw cow's milk to the breast fed infant during the new-born period.
3. By giving no raw cow's milk during convalescence from disease and during and after gastro-intestinal disturbances.
4. By refraining from the use of excessive and exclusive milk diets.
5. By elimination of the use of injections of milk for nonspecific therapy.

SUMMARY

Hypersensitiveness or allergy to milk is of more frequent occurrence than is generally realized and not only causes mild symptoms but may even result in acute anaphylactic death. It occurs in adult life as well as in infancy and childhood. The soluble whey proteins of raw cow's milk, lactalbumin and lactoglobulin, are most often responsible for this condition; casein plays a negligible rôle. The pathogenesis, which is accounted for on the basis of acquisition and not of inheritance, suggests preventive measures. The treatment consists in the elimination of raw milk from the diet, replacement of it by denatured milk, and the establishment of tolerance by the slow and gradual introduction of raw milk.

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ABSTRACT OF DISCUSSION

DR. CHARLES G. KERLEY, New York: I am convinced that inheritance is a great factor in many of the cases and I have observed it repeatedly when it had been acquired congenitally through the use of foods by the mother. I believe that the allergic state constitutes a condition of systemic inferiority, a familial disorder due to an endocrine imbalance. The wide variety and the combination of allergic manifestations may be explained only through a common physiologic deficiency constituting an entity. I will give one instance out of many for my conclusion that there is a preallergic state. A mother reacts to milk. By a milk reactor I mean an individual who is made acutely or chronically ill by the use of raw milk. I have known milk reactors through four generations: mother, daughter, grand-daughter and great grandson. In infants and children it is through the nervous system that the most urgent evidence and signs are produced. I divide my allergic responses into four groups: First is the shock group. In one of my alarming cases, shock was by contact. I placed seven drops of milk on the tongue of a baby, aged 3 months. In a few seconds shock was extreme: slow respiration, extreme pallor and heart sounds were absent. It was with the greatest effort that she was resuscitated. I have seen one case of death from shock in a baby of 10 months. It came time to wean the baby and 2 ounces of milk was forced on it. The child immediately went into collapse and when I came on the scene the child was pulseless, unconscious and in extreme shock. It died in spite of every effort. The lesser divisions were those of allergic response because the milk, disagreeing with the child, produces gastro-intestinal disorders, colic and reactions other than those related to the gastro-intestinal tract, notably eczema. In giving up cow's milk it is either a matter of goat's milk or human milk in the shock cases, and of heating of milk in the ordinary gastro-intestinal type and the eczema. A greater degree of desensitization is produced in eczemas and in cases of milder reactions of a gastro-intestinal nature by prolonged heating. Better results are obtained from two or three or four hours oftentimes than from one.

DR. SAMUEL GOLDBERG, Philadelphia: Because of the increased amount of knowledge of the body response to the various food proteins, particularly those found in milk, we as clinicans are probably often baffled as to how to apply it to our daily pediatric practice. One has only to glance through that excellent critical review by Francis Scott Smith in a recent issue of the *Journal of Pediatrics* to see how varied are the studies of animal experimentation and how different the observations and results obtained. Pirquet and Schick probably pioneered our idea of allergy, but in the last few decades there has been a general awakening to its importance and to the part it plays in our knowledge of disease and bodily response. I feel that there probably exists too great a gap between the students of allergy and the pediatrician or internist. I feel that there must be a closer bond between fundamental studies made by such enthusiastic workers as Dr. Ratner and the clinical interpretation given to it by clinicians at the bedside. Dr. Ratner, by his case report of the 9 year old boy, has shown that the skin reaction to the various proteins, on which so much stress is laid, is definitely inadequate to serve as a guide in this complex problem. He has shown that this boy, who was negative in his skin reaction to casein and only moderately active to lactalbumin by the intradermal test, was so acutely sensitive to lactalbumin as to have symptoms of collapse and shock. Here this minute amount of protein produced only a faint reaction in the skin and yet was sufficient to produce a shock reaction in the lungs. There is a tendency to regard these cases as allergic and too often one steps aside from them and refers them to other men, who are studying them from the standpoint of protein sensitivity alone. The importance of most detailed history and clinical study is perhaps being overlooked. If this were done, it would lead to a better understanding of familial strains, environmental influences, neurogenic factors and the part that internal glandular secretions play in regulating the blood mechanism and peculiarities. I make this plea for more careful pediatric study of these cases not to minimize the work of Dr. Ratner and similar observers but to incorporate it into everyday clinical bedside study, so that it may not be lost.

DR. ALBERT H. ROWE, Oakland, Calif.: Dr. Ratner's conclusion that apparent casein allergy is usually due to traces of soluble milk proteins will need clinical consideration. In my work, those patients markedly sensitive to milk have not been able to tolerate even evaporated milk without mild or severe symptoms. Emphasis on beef elimination is necessary in certain patients, and also butter at first. In such cases a soy bean substitute, almond milk or goat's milk has been used in children, and in adults prolonged and complete elimination has been the rule. My experience assures me that milk sensitization is especially common in infancy and childhood and occurs in unappreciated frequency throughout life. In adults it may persist in a potential form. Its original manifestation, be it gastro-intestinal, cutaneous or bronchial allergy, often disappears or diminishes to reappear in later years in similar or different manifestations, such as migraine or toxemia. As with allergy to any food, that to milk may also establish itself in middle life or even in old age from causes such as overindulgence in the food, intermittent ingestion or its consumption during digestive upsets. Especially important of realization is

the frequency of negative skin tests to milk and other food proteins. This, of course, emphasizes the necessity of trial or elimination diets in many patients suspected of such allergy. The frequency of concomitant allergies to other foods and the possible development of inhalant allergies as months and years advance must be remembered. However, the tendency to develop either food or inhalant allergy may persist alone throughout life and seems to be intensified by inheritance. Likewise the tendency to develop specific manifestations, such as eczema, migraine or gastro-intestinal, nasal or bronchial symptoms, tends to run in families.

DR. GEORGE PINESS, Los Angeles: The question of heredity as discussed by Dr. Ratner this morning does not disprove the theory of the heredity factor in allergy even though he is able to sensitize individuals to milk. The inability to disprove heredity as a factor in the allergic individual is due to the individual's lack of knowledge of his family history. This is particularly true in the clinic cases and not uncommon in private practice. Therefore one should not be too prone to question the theory of heredity. The question of boiling, evaporating and altering milk has proved to be a real problem to all of us who do allergy, in that we find that results can be obtained in some cases with every type of alteration of milk whether by boiling or by evaporating. The question of milk sensitivity has attracted my interest particularly in eczema in children in whom there was a seasonal incidence of symptoms. I am now investigating the possibility of some relation to the fodder of the cattle from which the milk is derived. Milk sensitivities that clear up spontaneously have been most difficult to explain in that despite any method of treatment they will clear up but later show some other type of allergy. I believe that most spontaneous cures are the result of self desensitization due to the patient refusing that particular substance or food in his diet which causes these reactions.

DR. FRANKLIN P. GENGENBACH, Denver: Finkelstein, more than twenty-five years ago, showed that infants tolerated a combination of cow's milk casein combined with breast milk whey better than they did breast milk casein combined with cow's milk whey. Also, he was able to cure temporarily the skin manifestations of eczema in bottle fed infants by taking out the whey from the cow's milk. It might be interesting to learn from Dr. Ratner, in making his skin tests for milk sensitivity, the percentage of positive reactions that he gets to whole milk, casein and lactalbumin, and also whether there is any marked difference in the reactions between his scratch tests and intradermal tests, realizing, of course, that, in cases which show marked reaction to the scratch test, he probably would omit the intradermal test.

DR. BRET RATNER, New York: Dr. Kerley's cases of transmission from mother to daughter seem to bear out clinically my experimental observation that this transmission has gone through the placenta and not through the germ plasm of the male, so that I would regard those apparent cases of inheritance as actually congenital; that is, acquired in utero. The remarks of Dr. Piness about inheritance, I think, are consonant with mine. The one fact I am certain of is that inheritance has not been proved scientifically to be a factor. So far as allergy can be acquired, I am sure that the inheritance factor may be placed in the background. It must be realized that these conditions are due to the entrance of antigens and that measures are at hand for their prevention. With reference to the cow's fodder, I think that it is of interest and that if a child does become sensitive to cottonseed or corn in this manner, boiling of that particular milk will certainly rid it not only of the anaphylactogenic lactalbumin but also of these extraneous substances. I have nothing to add to Dr. Goldberg's remarks. With reference to the discussion of Dr. Gengenbach, I was most interested in looking up the old literature of the Viennese and French pediatricians, and I was astonished to see how much further advanced they were in an understanding of milk allergy than are the pediatricians of today. Anaphylaxis was discovered about 1902, and probably the subject was fresh in their minds in the years 1905, 1910, 1912 and 1914. I believe that my experimental observations bear out the clinical observations they made.

TREATMENT OF ACUTE AND CHRONIC BRUCELLOSIS (UNDULANT FEVER)

PERSONAL OBSERVATION OF ONE HUNDRED CASES OVER A PERIOD OF SEVEN YEARS

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In 1859 Marston [1] described a disease syndrome which he named Mediterranean or gastric fever. In 1886 Bruce [2] isolated an organism, which he called Micrococcus melitensis, from the spleen of a patient who was a victim of this disease. In 1897 Bang [3] isolated the organism which is the recognized cause of contagious abortion in cows. This organism is now called Brucella abortus. In 1914 Traum [4] isolated an organism which is now called Brucella suis, from the fetus of an aborting sow. Thus, three strains of Brucella now have been recognized. In 1918 Evans [5] suggested that these organisms were very closely related, both serologically and bacteriologically, and that Brucella abortus in all probability could infect man. In 1924 Keefer [6] isolated Brucella suis from a so-called case of Malta fever, and in 1925 Duncan [7] first isolated Brucella abortus from man. It would be impossible to state the actual number of persons infected with the various strains of Brucella occurring in the United States. It is, however, a statistical fact that 9,965 cases were reported up to Jan. 1, 1935, and that the disease is increasing.

CLINICAL SYMPTOMATOLOGY

Five clinical types have been commonly recognized: intermittent, ambulatory, undulatory, malignant and subclinical. However, I find considerable difficulty in classifying under these headings the 100 cases that I have observed. In many of these cases the symptomatology is so varied that any grouping is most difficult. Two general types may be recognized: (*a*) an acute type, arbitrarily defined to include those cases which run their full course, with or without treatment, within three or four months, and (*b*) a chronic form, in which symptoms persist for a longer period. Acute Brucella infection is characterized by fever, weakness, sweating, chilliness, occasional rigor and some form of pain, such as headache, backache and arthritic or abdominal pains.

These symptoms associated with anorexia, constipation, nervousness and occasional cough would suggest the diagnosis of brucellosis. If the disease is prolonged, there is also associated loss of weight and evidence of neurologic toxemia.

In chronic brucellosis, a part or all of these symptoms are present; but the neurologic symptoms become more manifest, and in my experience the majority of complications occur in this group. Evans [8] has recently pointed out the importance of the neurologic manifestations of this disease and that, before the diagnosis

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3. Bang, Bernhard: The Etiology of Contagious Abortion, Ztschr. f. Tiermedizin **1**: 241, 1897.
4. Traum, J.: Annual report of the Chief, Bureau of Animal Industry, U. S. Department of Agriculture, 1914, p. 30.
5. Evans, Alice C.: Further Studies on Bacterium Abortus and Related Bacteria, J. Infect. Dis. **22**: 580 (June) 1918.
6. Keefer, C. S.: Report of a Case of Malta Fever, Originating in Baltimore, Md., Bull. Johns Hopkins Hosp. **35**: 6 (Jan.) 1924.
7. Duncan, J. T.: Contagious Abortion and Undulant Fever, Brit. M. J. **1**: 554 (March 21) 1925.
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of chronic neurasthenia or psychasthenia is made, the possibility of chronic brucellosis should be considered.

Brucella has been recovered in pure cultures from a large variety of suppurative lesions, such as meningitis, salpingitis, purulent orchitis, empyema, purulent cholecystitis, acute spondylitis with abscess formation, and acute mastitis. Cultures taken from these lesions in the average clinical laboratory will give negative results because of the difficulty in growing Brucella. This organism in all probability has been a hidden causative agent in many so-called sterile abscesses.

LABORATORY DIAGNOSTIC AIDS

Laboratory data are invaluable as aids for diagnosis and prognosis in brucellosis. Early in my study I believed that agglutination in a dilution of 1 to 80 was necessary to confirm a diagnosis. But I know now that, even when the agglutination titer is low or absent, the patient may be a victim of this disease. Since 1932 I have employed a skin test as a confirmatory aid in diagnosis when there was very strong clinical evidence in the absence of agglutination. This is performed by the injection of from 0.02 to 0.04 cc. of Brucella antigen intradermally, another patient or the laboratory assistant being used as a control. Any vaccine on the market is a suitable antigen for the performance of this allergic reaction. I have been able to recognize six cases included in this group by this method. Simpson [9] states that the agglutinins are absent in the blood stream in 5 per cent of the cases.

Blood cultures for the isolation of strains of Brucella, as performed in the average laboratory, are unsatisfactory because of the difficulty in securing proper mediums and equipment. Diagnosis by culture is delayed because it is recognized that cultures should not be reported negative until incubated for a period of thirty days. A leukopenia is usually present. Eighty-five per cent of this group of patients presented a white blood count of less than 6,500. In the differential smears, 90 per cent of this group presented a relative lymphocytosis and 65 per cent showed a definite increase in mononuclear leukocytes. Some degree of secondary anemia was shown in 87 per cent. Huddleston [10] suggested the additional laboratory test of opsonocytophagic power of the blood. I believe that this test is quite reliable, but I doubt its practicability. I should think that it would have its greatest value in those cases in which there is difficulty in determining whether or not the patient has recovered. It should not be forgotten that approximately 15 per cent of the patients suffering from tularemia show a cross-agglutination reaction with the abortus organisms. Differentiation between the two conditions can be made, however, by agglutination absorption tests.

TREATMENT

Many attempts at specific treatment of this disease have been made. Favorable results have been reported for the intravenous use of mercurochrome,[11] metaphen [12] and acriflavine hydrochloride.[13] Cazalas,[14] Auricchio,[15] Cumston,[16] DeFinis,[17] Giuffrè,[18] Khaled,[19] Prausnitz,[20] Schilling,[21] Simpson [9] and Harris [22] have all reported favorable results with specific vaccine therapy.

Early in 1928 I became particularly interested in the use of vaccine and in 1929 [23] I reported ten cases that were cured by this method of therapy. I early enlisted the cooperation of a large veterinary laboratory of the Middle West for securing pathogenic strains of Brucella. These cultures, after being thoroughly tested for virulence, were incorporated into a vaccine, 50 per cent Brucella abortus bovine and 50 per cent Brucella abortus swine being used. This was standardized to nephelometer number three, which is approximately six billion organisms per cubic centimeter. This particular preparation was submitted to the Council on Pharmacy and Chemistry in 1929, and in its report of 1930 [24] acceptance was withheld until further clinical data were available. In 1932 [25] it was fully accepted.

Arbitrarily 0.25 cc. was chosen as the initial dose given intramuscularly. This dosage was increased 0.25 cc. every second or third day, depending on the clinical reaction of the patient. A maximum dosage of 1 cc. was never exceeded in the cases that I have treated. I found early that the subcutaneous method of inoculation was too frequently associated with local abscesses; I therefore changed to the intramuscular route of injection, which gives faster absorption and has been in my experience rarely so complicated. I have usually employed the deltoid muscle as the favored site for inoculation. I think it advisable that not more than seven inoculations should be given during a single course of therapy and that the dosage should not exceed 1 cc. The average number of inoculations in the 100 cases was 5.4.

In one case a spectacular result with intravenous vaccine was obtained. After treatment over a long period of time with subcutaneous injections of vaccine, without appreciable benefit, this patient was given one injection of 0.1 cc. intravenously, resulting in a prompt cure. The reaction was so severe, however, that since then I have never used the vaccine intravenously. The reactions observed are specific and occur only in individuals who have been sensitized through actual infection with Brucella. If there is no elevation of temperature or no accentuation of the patient's symptoms during the course of vaccine therapy, the diagnosis should be carefully checked, for it is doubtful whether the patient has brucellosis. In control cases I have found the vaccine to be a very poor nonspecific protein. There is also an associated definite specific local reaction, characterized by soreness, induration and redness.

I believe that so long as the agglutinins persist in the blood stream, or the patient has active fever, this

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25. Report of the Council on Pharmacy and Chemistry, J. A. M. A. **99**: 1262 (Oct. 8) 1932.

fever can be accentuated by the use of vaccine. This is the result of an allergic systemic reaction. Consequently, fever can be prolonged unnecessarily by too long continued treatment. If the subjective symptoms of the patient have definitely subsided, injections of vaccine may be discontinued even in the presence of a low residual temperature. There follows a gradual disappearance of the clinical symptoms, including the fever. There is also a gradual return to a normal blood picture. I have had numerous letters stating that the vaccine yielded poor results and that as soon as its administration was stopped the patient got well. I feel that the continued fever in such cases is due to overtreatment.

There are certain contraindications to vaccine therapy. Particularly is the elderly individual a poor subject. His general physical condition is usually such that any form of "shock treatment" is contraindicated. A myocardium which shows the degenerative changes of senility makes that individual a particularly poor risk. I have also advised against the use of vaccine in two cases in which subacute bacterial endocarditis existed as a complication. In one of these cases injections of vaccine had been given prior to my observation and this had had no effect on the condition.

In cases in which satisfactory clinical results have not been obtained early in the course of vaccine therapy, a thorough investigation may reveal the presence of some complication, such as suppurative disease in the gallbladder, sinuses and tonsils. It has been pointed out by Harris [22] that a thorough x-ray study of the teeth should be made for the existence of periapical infection.

During the course of active treatment with vaccine, the patients in this series received no other medication. They were usually kept under observation two or three days until a definite base line could be drawn as to their exact condition. In addition to vaccine therapy, all patients received a high caloric diet, with feedings between meals. This is very important in the handling of patients with prolonged fever. After the patient shows clinical signs of improvement, a tonic mixture particularly rich in vitamins was prescribed. A large number of such proprietary mixtures are on the market and I have no particular preference. Patients showing a blood picture of secondary anemia were given adequate amounts of iron, usually in the form of pills of ferrous carbonate, 45 grains (3 Gm.) daily.

RESULTS

The interpretation of the end results of any method of treatment applied to either acute or chronic brucellosis is difficult. The question often presents itself in a case in which there is apparent recovery "Is the patient well?" or "What are the criteria by which one can establish that the patient is cured?" In answer to these questions it may be stated that as the patient recovers from brucellosis:

1. There is a definite disappearance of his subjective symptoms.
2. There is an increase in weight.
3. There is a gradual disappearance of fever.
4. The agglutination titer of the blood diminishes.
5. The blood picture returns to normal.
6. The neurologic symptoms subside.

In the 100 cases reported none are included that have been under observation less than one year. Two deaths have occurred from a complicating subacute bacterial endocarditis in which Brucella was shown to be the etiologic organism. Short relapses have occurred in 11 per cent. These cases have required an additional course of vaccine therapy. One case remains unimproved after a period of one year, owing to a complicating chronic cholecystitis and also multiple periapical infections of the teeth. Five cases were recorded as quiescent at the time of my observation and no vaccine was recommended. Eighty-four cases were observed and treated in the hospital. The average hospital stay was twenty-two days. Readmission was necessary in eight cases for an additional course of vaccine therapy or treatment of known complications.

COMMENT

In view of the fact that all students of this disease have emphasized that there is a large number of cases unrecognized and untreated in the United States, I would urge that, in each laboratory where blood is taken for the Wassermann reaction, the rapid agglutination test be made on the same serums. Suitable antigen can be obtained from any veterinary supply company, and the test is performed by the addition of one drop of serum to a drop of antigen and, after mixing, a macroscopic agglutination occurs if the serum is positive. This test can be performed in any physician's office and offers a very practical and easy way of increasing the percentage of diagnosed cases in the United States. In 2,000 consecutive blood Wassermann serums observed at my laboratory, 2.6 per cent have shown positive agglutination with Brucella. Of course, some of these are quiescent cases. Sixteen of my active cases were recognized in this manner.

CONCLUSIONS

1. Brucellosis is on the increase in the United States.
2. Vaccine therapy offers the best available method of treatment of both acute and chronic brucellosis.
3. The rapid method of agglutination test should be done on all Wassermann serums.
4. Brucellosis should be considered as a possible etiologic factor in many cases of so-called neurasthenia.
5. Brucella may be found to be the etiologic organism in many so-called sterile abscesses, if proper investigation is made.

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ABSTRACT OF DISCUSSION

DR. HAROLD J. HARRIS, Westport, N. Y.: Within two and one-half years I have observed seventy-five cases of Brucella abortus infection. Only nineteen could be classified as acute, the remainder running a chronic course with little or no febrile reaction and never enough illness to require bed rest. One chronically ill woman aborted three times; from her uterine discharge Brucella abortus was isolated. Pallor is often striking, with or without anemia. Anemia may be profound. There is apt to be a marked tendency to alveolar abscess, one patient having had twenty-eight abscessed teeth. Too much confidence has been placed in the blood agglutination test for the diagnosis of undulant fever, acute or chronic. Physicians have been led to believe that an agglutination titer under 1:80 is of little or no clinical significance. No clinician familiar with undulant fever is misled by this idea. In eleven of my seventy-five cases of chronic undulant fever the agglutination test was entirely negative on repeated tests. These cases were diagnosed on positive skin tests and clinical evidence. Much harm has been done by the habit of laboratories of labeling as characteristic only agglutinations in 1:80 or higher dilutions. Regarding treatment, my experience coincides with that of Dr. Angle, vaccine having been the only method of proved value. A small percentage of my patients with chronic brucellosis, treated a year or more ago, have suffered mild relapses in

spite of what I considered adequate vaccine therapy. It occurs to me now that these patients might not have relapsed if their antibodies had been maintained at a high level for longer periods of time. With this in mind, I am now watching their agglutination titers more carefully during their vaccine therapy and giving any dose necessary to secure and maintain a higher titer and, when necessary, I give small doses of the vaccine intravenously with apparently satisfactory results. Severe reactions may follow the use of this route, but extremely small doses may be used with safety in those whose agglutinins will not increase with the subcutaneous or intramuscular route. This route was used with success in a woman of 83 with marked weakness of the heart muscle. One dose of 50,000,000 killed organisms was given. It seems probable that undulant fever is a relapsing or recurrent disease only because the presence of large amounts of antibodies in the blood is so fleeting; therefore the problem is to keep antibodies present for a period sufficient to outlive the infecting organisms. I agree with Dr. Angle's statement that a patient who does not show the typical reaction to vaccine during treatment probably does not have brucellosis. I believe that the vaccine may be used as a therapeutic test with full assurance that the patient who is not suffering from brucellosis will not react in any degree.

LYMPHOCYTIC, MYELOCYTIC AND MONOCYTIC NEOPLASMS

ROENTGEN DIAGNOSIS AND TREATMENT

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Since the establishment of the Lymphatic Tumor Registry by the American Association of Pathologists and Bacteriologists, eight years ago, much progress has been made in assembling, correlating and extending the knowledge of neoplastic conditions of lymphatic, hematopoietic and reticulo-endothelial tissues as evidenced by the recent publication of the registrar, Dr. G. R. Callender.[1] With these advances in the clinical, hematologic and pathologic aspects of this difficult group of neoplastic diseases there has been little attempt to collect and correlate the x-ray studies, although many reports of cases and groups of cases are found in the current literature.

This paper represents an attempt to gather and correlate some of these x-ray studies through a report of some of our own cases and the review of others from the literature furnishing typical examples in the various classifications discussed by Callender.[1] In a further effort to clarify the subject, the group of sympathetic neuroblastomas, which metastasize widely to lymph nodes, bones and bone marrow, are contrasted with the group under consideration. Callender's classification tracing the various diseases back to the stem cell of the lymphocyte, polymorphonuclear leukocyte and monocyte is used throughout.

LYMPHATIC LEUKEMIA

In lymphatic leukemia there is involvement of the lymph glands and structures throughout the body with an enormous increase in the lymphocytes. The lymph gland involvement is usually generalized and in many instances the liver and spleen are enlarged. In the lymph nodes there is a great proliferation of the lymphocytes so that there is obliteration of the node structure. The malpighian nodules of the spleen become enlarged to a considerable degree. The bone marrow may become more or less transformed into lymphoid tissue. Profound anemia usually is present from replacement of the normal bone marrow.

Roentgen examination is indicated in all cases of pain or swelling over the bones and joints. Craver and Copeland [2] report bone changes in six of eighty-six cases of lymphatic leukemia. They feel that bone changes are of more frequent occurrence in low grade lymphatic leukemia than in cases with a high white count. The incidence of bone changes was, in order of frequency, femur, humerus, pelvis, metacarpals, ulna and vertebrae.

There may be elevation of the periosteum due to infiltration beneath the periosteum, and this is sometimes followed by osteosclerosis from proliferation of new bone. Extensive generalized osteoporosis may sometimes be present without localized areas of destruction. Snelling and Brown [3] report bone changes at some stage of disease in eight of twelve children with lymphatic leukemia. Their most constant change was a rarefied area near the end of the bone adjacent to the epiphyseal line together with elevation of the periosteum. Poynton and Lightwood [4] and Taylor [5] report extensive periosteal changes in these cases. The former report elongated localized leukemic deposits in the ends of the bones, with absorption of the bony cortex about these deposits.

Occasionally in this disease masses are found in other organs, such as the gastro-intestinal tract. Mead [6] has recently reported a case with tumor masses throughout the stomach almost like diffuse polyposis; also masses in the small bowel and colon.

Mediastinal tumors in connection with lymphatic leukemia have frequently been reported. This has been called leukosarcoma by Sternberg,[7] who thought it was a true neoplastic tumor. Other authors believe it to be a part of the general leukemic process. Cooke [8] has reported nine cases of acute leukemia with large mediastinal masses. In these cases roentgen therapy promptly removed the masses, but in a short time the blood changes returned acutely. After this the roentgen therapy was of no avail and the patients died.

A number of cases of lymphatic leukemia associated with lymphosarcoma have been reported. These cases apparently begin as lymphosarcoma and later develop leukemic manifestations, often of the acute type. Evans and Leucutia [9] reported three cases of lymphosarcoma, which were treated by roentgen therapy with marked improvement. The patients later developed lymphatic leukemia and died. The authors believe that lymphosarcoma is transformed into lymphatic leukemia as soon as the bone marrow becomes involved by foci of lymphosarcoma.

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7. Sternberg, C.: Leukosarkomatose und Myeloblastenleukämie, Beitr. z. path. Anat. u. z. allg. Path. **61**: 75, 1916.

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9. Evans, W. A., and Leucutia, Traian: The Neoplastic Nature of Lymphatic Leukemia and Its Relation to Lymphosarcoma, Am. J. Roentgenol. **15**: 497-513 (June) 1926.

CASE 1.—L. P., a man, aged 35, admitted, Feb. 23, 1935, complained of weakness and substernal pain. The onset had occurred with insomnia and "cold in the chest," and cough but no sputum or hemoptysis. There was progressive weakness and dyspnea on exertion. Substernal pain developed, with coughing.

On physical examination the left side of the chest was more voluminous than the right, with restriction of movement on the left. There was impaired percussion with absent breath sounds on the left below the angle of the scapula. The abdomen was distended. The spleen was not felt. No lymph gland enlargement was present.

Laboratory examinations revealed the following: The Wassermann reaction was negative. Blood studies showed: hemoglobin, 82 per cent; red blood cells, 4,900,000; white blood cells, 9,200; differential count: polymorphonuclear neutrophils, 66 per cent; polymorphonuclear eosinophils, 8 per cent; metamyelocytes, 2 per cent; lymphocytes, 22 per cent; monocytes, 2 per cent.

Roentgen examination of the chest revealed a large collection of fluid in the left pleural cavity, with displacement of the mediastinum. After 1,200 cc. of fluid was removed, progress films showed widening of the mediastinum.

High voltage roentgen therapy was administered over the mediastinum and lumbar area, which resulted in disappearance of the mediastinal mass. Some fluid continued to form in the left pleural cavity. The patient improved and went home, March 16, but was readmitted several days later with exacerbation of the coughing, oozing of blood from the gums, paralysis of the left side of the face, and palpable glands in the cervical, axillary and inguinal areas.

Examination of the blood showed: red blood cells, 5,120,000; white blood cells, 101,000; hemoglobin, 80 per cent; polymorphonuclear neutrophils, 8 per cent; lymphocytes, 12 per cent; blast forms, 80 per cent. On succeeding days the white count increased steadily to 253,000, and slowly fell to 6,200 and then rose to 18,400 over a period of two weeks. The stools showed a positive guaiac test. During all this time the patient was treated with repeated blood transfusions.

A postauricular lymph node was removed for study. The normal follicular structure was entirely replaced by masses of lymphocytic type cells with abundant mitotic figures.

The patient continued to grow worse and died April 7. He suffered a pulmonary hemorrhage as a terminal event.

At necropsy the spleen and liver were somewhat enlarged. Multiple small discrete petechial hemorrhages were found both in the skin and in many of the internal organs. There was an area of hemorrhagic pneumonia involving the upper lobe of the right lung. The spleen showed replacement of the lymphoid follicles by masses of small, deeply staining lymphocytes. The kidneys contained areas of lymphocytic infiltration. There was infiltration of the mediastinal, mesenteric, retroperitoneal and inguinal lymph nodes. Sections of blue marrow were taken from the lumbar vertebrae, sternum and ribs. The marrow was hypertrophic, with enlargement of the marrow cavity and of the cortex. There was considerable replacement of the normal medullary elements by small deeply staining lymphocytes. The changes were indicative of acute lymphatic leukemia.

This would appear to be a case of lymphosarcoma, which after roentgen therapy developed an acute lymphatic leukemia. It is difficult, however, to be sure that this was not a case of lymphatic leukemia in an aleukemic stage when first seen and which passed into the leukemic stage after roentgen therapy. Webster [10] reported a case (case 3) which was very similar in its history and pathologic manifestations to those of case 1 reported here. He places it in the leukosarcoma group. He believes it probable that leukosarcoma, lymphosarcoma and lymphatic leukemia are different manifestations of the same disease.

The prognosis in lymphatic leukemia is uniformly bad but, in the chronic type, roentgen therapy may prolong life for a considerable period of time. The acute form is a rapidly progressive form of the disease resulting in death in from a few days to a few weeks. We believe that roentgen therapy is not indicated in these cases and may even hasten the time of death. The chronic cases are more amenable to roentgen therapy and these patients survive for from a few months to four or five years. We do not consider that roentgen therapy is as effective in lymphatic leukemia as it is in myelogenous leukemia.

10. Webster, L. T.: Lymphosarcoma and Allied Conditions, Johns Hopkins Hosp. Rep. **20**: 251-314, 1921.

MYELOGENOUS LEUKEMIA

There is a definite elevation of the white blood cells with a large proportion of myelocytes. Both the total count and the differential count are capable of wide variation. Extensive changes are found in the bone marrow with hyperplasia of the granular leukocytic elements and decrease of the red marrow. Myeloid transformation is present in the spleen and liver particularly and may occasionally be seen in other organs. Bone destruction is uncommon.

Cone [11] states that myelogenous leukemia resembles sarcoma in a fluid medium. He believes that the clinical and pathologic manifestations indicate it to be of a sarcomatous nature. Piney [12] also believes it to be a neoplastic process and to be more rapid in its course when composed of immature cells.

Roentgen examination of the bones reveals very few changes. Craver and Copeland [2] in a report of eighty-two cases found bone changes in only one case. There was mottling of the upper portions of the femurs, with central punched-out lesions. There may also be osteosclerosis. Early lesions may be missed by roentgen examination. At autopsy they found various stages of absorption of the spongy trabeculae and some erosion of the cortex. Erosions of medullary bone were found in stages that could not be demonstrated roentgenologically. These authors conclude, therefore, that changes shown by the roentgen examinations are late changes.

Roentgen therapy is, and has been for many years, the chief therapeutic agent for the control of this disease. In spite of brilliant temporary remissions, the course of the disease proceeds uniformly to a fatal termination. Irradiation is usually applied over the long bones, vertebrae, ribs and sternum in order to destroy the radiosensitive myeloid hyperplasia. Irradiation of the spleen is also indicated for reduction of its size and destruction of the pathologic blood cells. In certain instances in which it is enlarged by leukemic infiltration, the liver also should be treated. After each recurrence the response to irradiation is less than formerly, and finally a stage arrives in which all treatment is ineffectual.

CHLOROMA

Chloroma, or chloroleukemia, may be said to be a tumor-like hyperplasia of the parent cells of the leukocytes, primary in the bone marrow. It is more common in young males but cases in the fifth and sixth decades have been reported. Dock and Warthin [13] in 1904 definitely established the relationship of chloroma and leukemia. Some writers divide the disease into myeloid and lymphoid groups, but the consensus at present is that the lymphoid group is extremely rare or nonexistent. Swanson [14] and others have reported cases

11. Cone, S. M.: Leukemia—A Sarcoma: Bone Evidence, Arch. Surg. **14**: 542-533 (Feb.) 1927.
12. Piney, A.: The Neoplastic Nature of the Leukemic Process, Am. J. M. Sc. **169**: 691-696 (May) 1925.
13. Dock, George, and Warthin, A. S.: A New Case of Chloroma with Leukemia, with a Study of Cases Reported Since 1893, M. News **85**: 971, 1904.
14. Swanson, L. A.: Aleukemic Myelogenous Chloroma, Am. J. Dis. Child. **44**: 140-145 (July) 1932.

showing an aleukemic form of the disease. Some writers, however, state that these are only aleukemic stages and not aleukemic types of the disease.

Postmortem examinations have usually revealed widespread, green colored growths with a marked predilection for the periosteum, the dura and the ligamentous structures. Involvement of the cranial bones, ribs, sternum and long bones is frequently found. The bone marrow often has a greenish cast. Exophthalmos with hemorrhage into the eyelids is a characteristic picture and is usually caused by retrobulbar masses of leukoblastic tissue. Pleural involvement with effusion is common. The cells are large, undifferentiated, mononuclear cells designated as myeloblasts or large lymphocytes. A moderate degree of anemia is usually present.

Roentgen changes in chloroma are quite variable. In some reported cases rather marked destruction was seen in the long bones and occasionally bone proliferation was present. In one case there was a large area of destruction in the vault of the skull underlying a soft tissue tumor. Extensive periosteal changes are usually present over the long bones. This periosteal change may consist of elevation of the periosteum parallel to the shaft of the bone, or there may be striae perpendicular to the bone similar to the changes seen in osteogenic sarcoma. The bone changes are often seen near the ends of the diaphyses of the long bones. In some cases, widening of the mediastinum was present.

Washburn [15] reported a case of chloroma in a boy, aged 20 months, who was given roentgen therapy. This resulted in an apparent complete recovery. The child was still living and well at the time of the report two and one-half years after the administration of roentgen therapy. In case 2 we administered high voltage roentgen therapy, which lowered the white blood count but had little appreciable effect on the progressive course of the disease.

CASE 2.—M. F. DeC., a white youth, aged 17, admitted, March 19, 1931, complained of swollen, stiff joints and lumps on the head. The condition had begun seven weeks before with gradual swelling of the ankle joints and pain on motion. The joints were warm but not hot or red and not sore to the touch. Later the knees, then the elbows, became involved. Three weeks later the mandibular joints became involved so that the mouth could not be closed. At that time several teeth were extracted, with rather copious hemorrhage following the extraction. During the fourth week of illness, tumors developed over the head, which gradually enlarged. The eyes had been protruding for the past ten days, and there was marked edema of the lids. Loss of weight amounted to 25 pounds (11.3 Kg.) in seven weeks.

The history was otherwise negative, with the exception of an attack of rheumatism three years before.

On physical examination the patient presented a striking appearance, with marked exophthalmos and edema of the upper lids, and the presence of large, nodular, circumscribed, hard masses distributed over the skull, particularly in the parietal and occipital areas on both sides. There was a softer swelling over the zygomatic area, which increased the breadth of the face. The eyeballs were definitely protruded. Some nasal obstruction was present. The mouth was wedge shaped and there was swelling over the temporomandibular articulations and the maxilla.

There was general lymphatic adenopathy. The liver and spleen were easily palpable. There was a globular enlargement over the lower end of the left humerus.

The physical examination was not of interest otherwise, except for a few vague changes in the chest. The blood pressure was 130 systolic, 50 diastolic.

Laboratory examinations showed: red blood cells, 3,350,000; hemoglobin, 48 per cent; white blood cells, 24,200; polymorphonuclears, 4 per cent; small lymphocytes, 7 per cent; large mononuclear leukocytes, 4 per cent; myeloblasts, 83 per cent. The myeloblasts varied from 8 to 20 microns in diameter. The nucleus was unusually large, the cytoplasm being represented by a rim of darker staining granular material. The nucleus stained lightly with Wright's stain and often appeared polymorphous or definitely lobulated. With the oxydase stain, the majority of the myeloblasts showed blue-staining granules in the cytoplasm.

The Wassermann reaction was negative. The phenolsulphonphthalein test showed a return of 27 per cent in two hours.

Roentgen examination disclosed the following changes: In the skull there were multiple pinhead sized radiolucent areas through the vault, and an irregular fuzzy type of decalcification of the facial bones. There was a collection of fluid in the right pleural cavity. The right lung showed extensive infiltration. Practically all the bones showed evidence of an infiltrative lesion with an osteoporosis having a granular appearance. There were areas of bone destruction in the shafts of the humeri near the upper epiphyseal lines. Periosteal reaction was seen over many of the long bones. Around the left elbow there were raylike striae perpendicular to the bone, and similar but less marked changes were seen around the knees. We felt that the whole picture was that of a blood dyscrasia of an undetermined type.

The patient's general condition continued to decline in spite of blood transfusions and general medical care. The temperature ranged from 99.5 to 103 F.

The blood calcium was 11.5 and the blood sugar 91 mg. per hundred cubic centimeters. The urine was negative for Bence-Jones bodies.

A gland was removed for examination. It was definitely green. Microscopically it showed loss of the normal lymph gland architecture. The tissue was composed of cells of the myelogenous type, which were usually large and had pink-staining and round or oval bilobed and polymorphous nuclei. Mitosis was quite marked. A diagnosis of chloroma was made.

March 31, roentgen therapy was started and one-half erythema dose was given over the head, cervical areas, shoulders, elbows, inguinal areas and one area over the spleen; 0.5 mm. of copper plus 1 mm. of aluminum filtration with 185 kilovolts at 50 cm. distance was used.

During this treatment period the patient's general condition improved to a marked degree, and on the last day of treatment the white blood count was 20,500. Two days later the count dropped rapidly and declined to as low as 1,500, but under repeated small transfusions gradually came up to 2,800. At this time an area of gangrene developed with ulceration at the gingivobuccal fold of the left lower mandible. This progressed in spite of medical care and eventually sloughed through the cheek.

The patient seemed to improve temporarily and the fluid in the chest cleared up. After a short time the condition became worse and the patient died one month after the high voltage roentgen therapy. At that time the white count was 24,500. Autopsy was not permitted.

It is apparent that this was a tumor closely connected with leukemia and may be properly considered as a subvariety or form of myelogenous leukemia. Practically all the well studied cases reported during the past twenty years have been of myelogenous origin.

These cases, in addition to the blood picture, are characterized by green tumors in almost every part of the body and in many cases they cause exophthalmos by tumors behind the eyeballs. Bone involvement and periosteal reaction, sometimes perpendicular to the bone as in osteogenic sarcoma, are found on roentgenographic examination. General glandular enlargement is found, together with enlargement of the spleen and liver.

Practically all cases reported in the literature ended fatally, with the exception of one patient who was living

15. Washburn, A. H.: Chloroma: Report of a Case with Recovery Following Roentgenotherapy, Am. J. Dis. Child. 39: 330-348 (Feb.) 1930.

and well two and one-half years following roentgen therapy. Case 2 showed some improvement with clearing up of the pleural effusion, following roentgen therapy.

ALEUKEMIC MYELOSIS

There are certain atypical cases of generalized myeloid hyperplasia of the bone marrow and viscera in which the white blood count and differential count are practically normal. If immature forms are present in the blood stream, they occur at such irregular intervals or in such low numbers that they are of no diagnostic value. There is usually a definite anemia present. Aleukemic and leukemic myelosis are in many instances indistinguishable by histologic examination.

Baldridge and Fowler [16] state that 5 per cent of their patients with diffuse myelosis were permanently aleukemic. They believe that the aleukemic form of myelosis may be more rapidly fatal and may have a greater degree of associated anemia and more likelihood of secondary hemorrhagic purpura than the leukemic form. Splenomegaly is a striking clinical finding.

The roentgen changes are of considerable importance in the differential diagnosis. The bone changes may be either osteolytic or osteosclerotic. The osteolytic type may easily be mistaken for multiple myeloma, as in case 3, or it may suggest metastatic carcinoma. Baldridge and Fowler's [16] case 4 showed only a single area of osteolysis in the mandible. In their case 5 there were multiple areas of bone absorption together with subperiosteal proliferation parallel to the shaft of the bone. There were also perpendicular striae found near the muscle and tendon attachments of numerous bones. In the spine, the lesions were osteoblastic in type. In the cranial bones there were multiple pinpoint areas of decalcification. Their case 6 showed evidence of rarefaction round the distal ends of the long bones, with a generalized osteoporosis. Stephens and Bredeck [17] reported two cases presenting generalized osteosclerosis which were indistinguishable from metastatic carcinoma of the osteoblastic type.

Therapy in this group of cases is of no avail. Jaffé [18] quotes various authors to the effect that splenectomy always seems to be fatal, the patients dying during the operation or soon after. He also states that irradiation of the spleen seems to be of no avail. In one case reported by Baldridge and Fowler [16] irradiation was applied to a nodule on the forearm with about 75 per cent reduction in size in seventy-two hours.

CASE 3.—A. B., a white woman, aged 51, admitted, Aug. 28, 1934, complained of pain in the back, loss of weight, and weakness.

The patient's father died of a tumor at the age of 40. Her past history was negative in relation to her present illness.

She dated the pain from September 1933 while watching boat races. This grew worse in a month and spread all over the spine and to the shoulders and neck. The pain did not seem any worse than at the beginning of her illness. She had lost 44 pounds (20 Kg.) since October 1933. There had been progressive weakness since the onset of symptoms.

The patient was moderately emaciated and quite pale. The chest was barrel shaped and somewhat deformed, as if from previous rickets. The heart was slightly enlarged. No abdominal masses could be palpated. There were a few palpable glands in the cervical and inguinal areas. Limitation of motion of the shoulders was present. There was exaggeration of the dorsal kyphosis. Marked weakness prevented the patient from standing.

Laboratory examination revealed: Wassermann reaction, negative; red blood cells, 3,120,000; white blood cells, 13,100; polymorphonuclear neutrophils, 73 per cent; polymorphonuclear eosinophils, 1 per cent; small lymphocytes, 21 per cent; large lymphocytes, 2 per cent; transitionals, 3 per cent; hemoglobin, 9.4 Gm. Moderate poikilocytosis was present. The blood calcium was 13.67 mg. and phosphatase, 4.55 mg.

Roentgen examination showed marked osteoporosis of the cervical vertebrae and osteoporosis, with narrowing of several of the dorsal and lumbar vertebrae. The ribs and scapulae also showed osteoporosis, with areas of destruction throughout these bones. Similar changes were seen in the pelvis and femurs. The skull was the seat of multiple areas of destruction scattered throughout the cranial vault. These areas varied in size from a few millimeters to 2 cm. The impression was that this case was probably one of multiple myeloma.

The patient steadily declined and died, September 18.

At autopsy, in each kidney a tumor mass was found. These were rubbery in consistency and suggested an infiltrative mass, since the margins were not sharply delimited. A few enlarged retroperitoneal glands were found and on section resembled the kidney lesions. In the bodies of the lower dorsal and lumbar vertebrae the bone marrow was replaced by grayish, friable, granular material suggesting leukemic involvement. There was marked decalcification of all the bones. The essential bone lesion appeared to be a rarefaction of bone structure with thinning of the cortex together with replacement of these structures by grayish, friable, very cellular tissue.

Microscopic examination of the lymph nodes showed the normal lymphatic structure almost entirely replaced by cells derived from the granulocytic elements. There were myelocytes and myeloblasts and polymorphonuclear leukocytes. There were also large multinucleated giant cells, which resembled megakaryocytes. The remaining cells were lymphocytic and monocytic in nature. Similar cellular elements were observed in the kidney lesions. The material from the bone marrow was made up of closely packed masses of myelocytic cells with stroma. These included not only myelocytes but also myeloblasts and partially obscured polymorphonuclear leukocytes together with occasional large, multinucleated pink-staining megakaryocytes. An occasional erythroblast was seen. A diagnosis was made of diffuse aleukemic myelosis involving the vertebrae, ribs, sternum, kidneys, spleen, retroperitoneal lymph nodes, and liver.

HODGKIN'S DISEASE

Hodgkin's disease is characterized by painless progressive lymph node enlargement, often beginning in the cervical groups. It is frequently accompanied by fever, and in later stages by anemia and cachexia. The blood changes are not diagnostic, although there is usually a slight leukocytosis as the disease progresses. There may be an increase in the eosinophils and lymphocytes. The blood platelets are usually increased.

The glandular involvement may be local or it may involve all the lymph glands of the body. The spleen is frequently involved and enlarged. The liver is less often affected. Cutaneous manifestations are common and quite annoying, because of pruritus.

The bone marrow may be involved rather frequently. Krumbhaar [19] has reported a case with involvement of the bone marrow and spleen without involvement of the lymph nodes. Craver and Copeland [20] reported twenty-seven cases of demonstrable bone changes (15.7 per cent) in a series of 172 proved cases of Hodgkin's disease. They report the incidence of osseous changes from other authors' reports as varying from 10.7 per

16. Baldridge, C. W., and Fowler, W. M.: Aleukemic Myelosis, Arch. Int. Med. **52**: 852-876 (Dec.) 1933.
17. Stephens, D. J., and Bredeck, J. F.: Aleukemia Myelosis with Osteosclerosis, Ann. Int. Med. **6**: 1087-1096 (Feb.) 1933.
18. Jaffé, R. H.: Aleukemic Myelosis, Arch. Path. **3**: 56-72 (Jan.) 1927.
19. Krumbhaar, E. B.: Hodgkin's Disease of Bone Marrow and Spleen Without Apparent Involvement of Lymph Nodes, Am. J. M. Sc. **182**: 765-769 (Dec.) 1931.
20. Craver, L. F., and Copeland, M. M.: Changes in the Bones in Hodgkin's Granuloma, Arch. Surg. **28**: 1062-1086 (June) 1934.

cent to 34 per cent. Pain usually preceded discovery of the bone lesions, although in some cases the lesions were discovered accidentally by roentgen examination. In a review of the literature they found the following bones involved in the order of their frequency: vertebrae, sternum, pelvis, femur, ribs, skull, humerus, scapula and clavicle.

Roentgen examination discloses both osteoclastic and osteoplastic lesions. In the spine the two types of lesions may be present in the same case. When osteoclastic lesions are present there may be collapse of the affected vertebrae, with considerable deformity. In one of our cases the collapse occurred when the patient was sitting up in bed. The disks are usually unaffected. The pelvis may show rather extensive osteolytic lesions with large, cystic-like areas interspersed with areas of eburnation. Pfahler and O'Boyle [21] reported a case of sacro-iliac involvement, which cleared up under roentgen therapy. We have recently had a patient with similar involvement, which cleared up similarly under roentgen therapy.

Lesions of the long bones are apt to begin in the proximal ends. In some instances the lesions are exactly similar to metastatic malignant growths of the osteolytic type, while in others there is evidence of sclerosis surrounding faintly visible areas of bone destruction. There may be some periosteal thickening. The ribs show similar punched-out areas of bone destruction. Lesions of the skull are apt to be osteoclastic.

Roentgen therapy is the most effective agent in the treatment of Hodgkin's disease. Radium therapy may be used but is not economical as to time or expense, and the final results are practically the same. The method of applying the radiation therapy varies as to dosage applied, voltage and filtration; also as to the number of areas treated. Desjardins [22] prefers the use of from 135 to 140 kilovolts filtered through 4 to 6 mm. of aluminum. He also advocates treating all the bodily lymph nodes even though only part of them have demonstrable involvement. Leucutia [23] uses voltages from 160 to 200 kilovolts filtered through copper or zinc and exposes only the actually diseased areas. Craver and Copeland [20] advocate high voltage applied in either suberythema or fractional doses, depending on the local and general condition of the patient. We use from 180 to 200 kilovolts filtered through 0.5 mm. of copper applied in suberythema doses when the patient is in satisfactory condition; otherwise, fractional dosage is used. We treat only the areas of demonstrable involvement because we consider that the disease has a hopeless prognosis, and excessive irradiation may cause leukopenia and severe anemia in a patient who is in need of all his bodily defenses. Craver and Copeland [20] have aptly stated the case: "The treatment regarded as best is that which will secure the best palliation for the longest time. The treatment should never be so severe as to make it seem harder to bear than the disease." Leucutia [23] states that the five year survival group mounted to from 15 per cent to 33 per cent. In 8 per cent of the cases there is a ten year survival. In addition there is considerable symptomatic improvement.

21. Pfahler, G. E., and O'Boyle, C. P.: A Case of Hodgkin's Disease, with Late Development of Sacro-Iliac Disease Cured by Roentgen Treatment, Am. J. Roentgenol. **11**: 406-410 (May) 1924.
22. Desjardins, A. U.: Radiotherapy for Hodgkin's Disease and Lymphosarcoma, J. A. M. A. **99**: 1231-1236 (Oct. 8) 1932.
23. Leucutia, Traian: Irradiation in Lymphosarcoma, Hodgkin's Disease and Leukemia, Am. J. M. Sc. **188**: 612-623 (Nov.) 1934.

CASE 4.—F. C., a white man, aged 40, admitted, Nov. 17, 1934, complained of swelling of the neck and low back pain. Examination revealed a large mass of glands in the right cervical area. There was also enlargement of the axillary and inguinal glands. Some tenderness was elicited over the lower part of the back. The blood studies were negative. Biopsy of an axillary gland resulted in a diagnosis of Hodgkin's disease. Roentgen films of the chest showed widening of the upper mediastinum.

High voltage roentgen therapy was administered over the cervical, inguinal, axillary and mediastinal glands and also over the lumbar spine. From 190 to 200 kilovolts was used and from 560 to 696 roentgens per field was administered. This resulted in disappearance of the glands in one month, but the patient continued to feel bad.

May 13, 1935, he was readmitted. On examination a few superficial glands were felt. There was a large mass in the upper part of the abdomen apparently continuous with the liver and extending below the umbilicus on the right side. The spleen was not felt. Roentgen examination at that time revealed fluid in the right pleural cavity. There were punched out areas of bone destruction in the right scapula and several ribs. There was also involvement of the dorsal and lumbar vertebrae, with areas of destruction, and extensive decalcification of many of the vertebrae. There was also extensive involvement of the bones of the pelvis and upper portion of the right femur.

May 21, when the patient sat up in bed, he had a feeling that his spine gave way and marked tenderness was elicited over the midlumbar area. Roentgen examination showed definite narrowing of the seventh dorsal vertebra.

LYMPHOSARCOMA

Lymphosarcoma is similar in many of its clinical aspects to Hodgkin's disease and it may be difficult to separate the two. It often involves a somewhat older group in general. There is less likelihood of an accompanying fever, and it is more radiosensitive than Hodgkin's disease. Lymphosarcoma frequently involves parts of the gastro-intestinal tract and peritoneum. Microscopic examination of an excised gland is necessary to establish the exact diagnosis.

Bone involvement in lymphosarcoma is not nearly so common as it is in Hodgkin's disease. The roentgen changes are similar, however. There are sometimes osteolytic lesions of the long bones with pathologic fracture. Occasionally periosteal lesions are seen. Pohle and Ritchie [24] reported a case of lymphosarcoma of the femur in which a pathologic fracture was sustained. There were areas of involvement in the left femur, right ilium, right radius, right parietal bone and several ribs. There were areas of increased bone density as well as areas of osteolysis. At autopsy widespread lesions were found. In the ribs there were fusiform osteolytic lesions with pathologic fractures. Microscopically it proved to be lymphosarcoma. Leucutia [23] found the cortex intact in his cases, except for occasional areas of invasion. He believes that this respect for the cortex by lymphosarcoma explains the rarity of roentgen changes in the bones. Histologically he found replacement of the bone marrow by tumor tissue and later gradual destruction of the normal bone marrow tissue.

In this disease roentgen therapy is also of prime importance. While lymphosarcoma almost universally causes the death of the patient, there are a few patients who have lived for a period of over ten years and who should probably be put in the category of cured cases. The average length of life in treated patients varies from two to four years. Approximately from

24. Pohle, E. A., and Ritchie, G.: Lymphosarcoma of the Femur, Radiology **18**: 635-637 (March) 1932.

15 to 20 per cent will live five years. The reticulum cell type of lymphosarcoma is somewhat more resistant to radiation than the lymphocytic type, and the results show a shorter span of life. We prefer the use of from 180 to 200 kilovolts filtered through 0.5 mm. of copper plus 1 mm. of aluminum, and the administration of suberythema doses to the affected glands. We do not treat the areas in which involvement was not demonstrated, except in certain cases in which we have reason to believe that there may be involvement of the retroperitoneal nodes. In the abdomen, definite verification may be difficult to obtain unless the glands are quite large. The usual medical supportive measures should also be carried out in all these cases.

MONOCYTIC LEUKEMIA

Monocytic leukemia is a third type of leukemia about which there is no very general agreement as to its separate entity. It is characterized by an increase in the number of monocytic cells associated with extensive growth of the reticulo-endothelial cells in the various tissues. Most of the cases have been of an acute type lasting from a few weeks to several months. Pronounced anemia and some fever are usually present. There is elevation of the white blood cell count, with from 50 to 75 per cent of the cells being monocytes.

Postmortem studies show enlargement of the liver, spleen and lymph nodes. There is often involvement of the kidneys, adrenals and other viscera. In some reported cases tumor masses have been found similar to those in chloroma. The bone marrow is usually hyperplastic and there are groups of monocytes present which are not seen under normal conditions.

Very little information can be gained from the literature in regard to possible roentgen changes in the bones. Osgood and Lyght [25] have reported two cases in which roentgenograms were made of several bones but nothing suggestive was found. Doan and Wiseman [26] also found no roentgen evidence of pathologic changes of the bone in one of their cases. The same authors tried roentgen therapy in several of their cases with very little beneficial effect. Dameshek [27] also tried irradiation in a case without any considerable benefit.

COMMENT

In reviewing the roentgen changes in the bones of these cases, one cannot help but be struck by certain points of similarity in the various diseases.

Periosteal changes are of two types: (1) elevation of the periosteum with calcification parallel to the shaft of the bone, and (2) raylike striae perpendicular to the bone. In the diseases under consideration we find the parallel type of periosteal change in lymphatic leukemia, aleukemic myelosis, chloroma and Hodgkin's disease. In myelogenous leukemia and lymphosarcoma no similar changes were reported; but there are very few reported cases in the literature, so that it is possible that they might show this change. In the second type with perpendicular striae, these changes were found in chloroma and aleukemic myelosis. This was quite a striking finding in our case of chloroma and was very similar to the raylike changes that are seen in osteogenic sarcoma.

Bone destruction may be classified under several headings: 1. Punched-out areas of bone destruction. This type of lesion was present in myelogenous leukemia, aleukemic myelosis, chloroma, Hodgkin's disease and lymphosarcoma. 2. Bone erosion in the ends of the diaphyses of the long bones. This was found in lymphatic leukemia, aleukemic myelosis, chloroma and Hodgkin's disease. 3. Pinpoint areas of decalcification or destruction. These were seen in aleukemic myelosis and chloroma and were usually in the flat bones, particularly in the skull. 4. Erosion of the cortex from within the medullary canal. This was reported from pathologic material of myelogenous leukemia by Craver and Copeland,[2] who believed that it was rather difficult to demonstrate on the roentgenogram and considered it a late lesion.

Osteosclerosis was also a prominent finding in these diseases. It may be a generalized condition, as is seen in aleukemic myelosis, or may be present in certain locations, as is seen in Hodgkin's disease and myelogenous leukemia. It is seen occasionally in lymphatic leukemia.

Generalized osteoporosis has been seen in lymphatic leukemia, aleukemic myelosis, and chloroma. In some cases of long standing this might be atrophy from disuse, but there would also appear to be some cases presenting this sign due to the disease itself.

From this summary of bone changes it would seem that there are no characteristic changes that would lead one to differentiate these rather uncommon diseases roentgenologically. We have found, however, that the periosteal changes in conjunction with the peculiar moth-eaten areas of erosion at the ends of the diaphyses —usually at the proximal ends along the medial border —are changes that are rather uncommon in other diseases. When these are associated with the pinpoint areas of decalcification in the flat bones, one should suspect some myeloid or lymphoid neoplastic condition.

We have recently studied three cases of sympathetic neuroblastoma that show practically the same roentgen changes as the diseases under consideration. There were extensive areas of destruction in the long bones and areas of erosion at the proximal ends of the diaphyses. Considerable localized osteoporosis was present near the ends of the long bones at the knee joints in one case. Pinpoint decalcification in the skull was present, together with larger focal areas of destruction in the pelvic bones, ribs and scapulae. It would be very difficult from the roentgen picture alone to differentiate these cases from the neoplastic diseases. These cases will be reported in detail elsewhere.

In the differential diagnosis one must consider metastatic carcinoma, multiple myeloma, osteogenic sarcoma, xanthomatosis, Gaucher's disease, Albers-Schönberg's disease, and bone infections.

Therapy in these conditions is mostly concerned with irradiation, although the usual medical supportive measures are indispensable. In the acute form of lymphatic leukemia, irradiation is contraindicated and may even be harmful. In the chronic form startling remissions occur, but the prognosis is uniformly bad. The same may be said of myelogenous leukemia, although the span of life is somewhat longer and the morbidity is usually less. In aleukemic myelosis there is no treatment that gives even temporary satisfactory results, although this may be due to the fact that very few cases are diagnosed ante mortem and, therefore, no large statistics on therapy are available. One patient with chloroma

25. Osgood, C. W., and Lyght, C. E.: Monocytic Leukemia, J. Lab. & Clin. Med. **18**: 612-626 (March) 1933.
26. Doan, C. A., and Wiseman, B. K.: The Monocyte, Monocytosis, and Monocytic Leukosis: A Clinical and Pathological Study, Ann. Int. Med. **8**: 383-416 (Oct.) 1934.
27. Dameshek, William: Acute Monocytic Leukemia, Arch. Int. Med. **46**: 718-740 (Oct.) 1930.

was alive and well two and one-half years after radiation therapy, but no other case could be found in which the progress of the disease was arrested by any method of treatment. High voltage roentgen therapy is the method of choice in both Hodgkin's disease and lymphosarcoma. A considerable symptomatic improvement and temporary abeyance of the disease process is achieved in many cases by this method of therapy. The average length of life in these cases is definitely raised and in a very few cases one may use the term cure.

PROGRESS AND PROBLEMS IN ENDOCRINOLOGY

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So rapid has been the progress in endocrinology during the past few years that selection of material for special consideration presents a difficult task. Hundreds of sound studies have been carried out and of these perhaps not one is without significance to pediatricians. Some, however, are of more immediate interest than others.

IMPORTANCE OF THE THYROID GLAND

Despite the wealth of new information about other glands, the thyroid gland still remains the most important to the practitioner in that thyroid problems are most easily recognized and the thyroid hormone is the most readily available and most effective for therapeutic purposes. The thyroid gland exercises a twofold function. In childhood it has a widely pervasive influence on the anabolic processes. Neither growth nor differentiation can take place in any adequate degree without the agency of the thyroid hormone. Thus, in thyroid deficiency there are seen all the well known abnormalities of physical and mental development and, as a result, poverty of the personality.

In the franker manifestations these effects are unmistakable and need no further elucidation. Thyroid deficiency, however, is manifested in all degrees from outspoken myxedema to complete normality. It is important to remember, as Shelton says, that "if physicians depend upon myxedema as the essential feature in the diagnosis of thyroid insufficiency at any period of life, then they must overlook the majority of hypothyroid sufferers."

There are a large number of cases of thyroid deficiency in children in which the gross signs of the condition, such as myxedema, dwarfism or obesity, are not apparent. Typically, the picture consists of moderate or slight delay in growth, teething and skeletal development; mental retardation; dry and brittle hair; poor nutrition and sluggish functions of the skin; constipation; emotional instability, disturbed sleep, capricious appetite and intractability; painful muscles and joints, and, what is especially illuminating, failure to respond to dietary treatment. An important cause of anemia that is rather commonly overlooked is thyroid deficiency. Frequently accompanying this are weakness and weariness. Menorrhagia and metrorrhagia in girls are not infrequently to be ascribed to this same cause. Several of the dermatoses can at times be traced back to thyroid hypofunction. Lesser degrees of nervous involvement are seen as forgetfulness, inattentiveness and restricted initiative. Lisser is authority for the statement that thyroid deficiency also with significant frequency plays a causal rôle in certain diathetic manifestations in infants, including vomiting, intestinal colic and even megacolon and ascites. In short, neglect to consider this gland leaves many a pediatric problem only partially, if at all, solved.

The simultaneous occurrence of any two or three of the manifestations just listed should throw suspicion on the thyroid gland. The most direct aid toward the recognition of the glandular agency in the symptomatology is a study of carpal development as disclosed in roentgenograms. An elevation of the blood cholesterol content is also of some diagnostic significance, but so wide is the normal fluctuation of the titer that no great dependence can be placed on it. Often a therapeutic test with desiccated thyroid in small doses gives illuminating results. Variations in the creatine output are also worthy of further study for their diagnostic significance.

Little need be said at this juncture of the catabolic effects of the thyroid hormone. Occasionally these are seen in clinical manifestation in the early years, as in cases of exophthalmic goiter, and therapeutically this property is occasionally of use in the treatment of obesity. The stimulating properties of the thyroid hormone can be utilized further in case of a variety of deficiencies involving other endocrine glands. There is direct evidence that some of these glands are susceptible of stimulation by this agent, and there is presumptive evidence that this is true also of others. Despite the well grounded objections to glandular polypharmacy there is a sound basis for the addition of thyroid substance to a variety of other glandular products when it is desired to use not only substitution therapy but also supplementary glandular stimulation.

Perhaps an apology should be offered for reiterating these matters, as they have often been discussed in the medical literature. Nevertheless many physicians are disinclined to profit by them because of an exaggerated fear of thyroid medication. Despite the fact that the best way to place an endocrine gland at rest is to administer its active principle, there is a widely held misgiving that thyroid medication may give rise to exophthalmic goiter. While the efforts of physicians to protect the public from dangerous dosing with thyroid derivatives is commendable, it is time, as Lisser says, that the exaggerated fear of this valuable medicament should be assuaged. It is doubtful if any other product listed in the pharmacopeia when properly used is less harmful or more valuable.

Thyroid should be prescribed initially in small doses, preferably no more than one-fourth grain (0.02 Gm.) of desiccated substance a day. If the patient happens to have a very low titer of circulating thyroxine, even this dosage may evoke an overreaction. This is frankly manifested as nervous tension and often tremors and lacrimosity—in short, the patient becomes "jittery." Such a reaction to small doses is, to my mind, pathognomonic of thyroid deficiency and indicates an imperative demand for continuation of the treatment. After a few days' rest it should be resumed at a level of one-tenth grain (0.006 Gm.) daily and gradually increased to the empirical optimum for the patient. The characteristic lag of the reaction and the cumulative effect must be kept in mind. It is also important to

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realize that the patient whose tissues are starving for thyroid may have only a narrow zone between two little and too much; hence until the organism becomes adjusted the dosage must be carefully regulated. In this respect every patient is a law unto himself.

OTHER ELEMENTS IN THE PROBLEM OF ORIENTATION

Today the pituitary body is in the focus of medical attention. From this gland are derived a variety of active substances that influence an astonishing number of physiologic functions. That it contributes importantly to growth has been known for many years. Also familiar now is the fact that sexual development and the continuation of sexual activity are dependent on pituitary hormones. For the growth hormone Evans has recently proposed the designation somatotropic. The promotion of sexual activities seems to depend on two gonadotropic factors, one of which stimulates the gametogenic tissues and the other the interstitial tissues of the primary gonads. The morphologic integrity of the thyroid gland as well as its continuing function depends on another principle, the thyrotropic. Similarly, an adrenotropic hormone preserves the integrity of the adrenal glands.

All of these relationships are of course important factors in the everyday work of the pediatrician. Of somewhat special pediatric interest is the recently discovered mammotropic hormone, which has been especially studied by Riddle. It is this agent that sets into activity the ripened mammary glands of the mother. It is due to the beneficent influence of this hormone that problems of infant feeding are usually automatically solved. Riddle's more recent work has suggested, too, that the mammotropic hormone plays a considerable rôle in the setting up and maintenance of the maternal instincts. Under its influence virgin rats have been made to adopt and mother not only infant rats but also mice, squabs and rabbits. The part that it may play in human psychology presents a problem worthy of consideration. One of the most surprising developments of the past two years is the discovery that the anterior pituitary body plays an important part in the regulation of sugar metabolism. It has now been sufficiently demonstrated that experimental diabetes can be prevented or largely ameliorated by the extirpation of the pituitary gland. This discovery logically compels a restudy of the entire problem of diabetes with due regard to the interglandular relationships. The pituitary gland plays a part, too, in fat metabolism and probably in water metabolism. These are a few of the primary influences of pituitary hormones that can now be recognized. The secondary influences present an almost bewildering array of problems as yet largely untouched and demanding intensive investigation.

Growing enlightenment is increasing the importance that must be ascribed to the adrenal cortex. Deficiency of its secretion retards growth as well as mammary activity; hence it must be considered as a hitherto neglected factor in feeding problems. Firor and Grollman's recent discovery that one of the cortex hormones can be adsorbed on charcoal, in which form it is effective when administered by mouth, promises to be a discovery of major clinical significance. Work in our laboratory (by J. M. Looney) has disclosed an active extract that is apparently neither epinephrine nor so-called cortin, an adrenal cortical extract, and that has a marked pressor influence. This may prove to be of importance in the treatment of conditions of circulatory asthenia.

Of special interest to the pediatrician is also the recent discovery of the potency of Hanson's extract of the thymus. Several generations of rats have now been treated with astonishing increasing stimulation of infantile development. While it is true that the work hitherto reported by Rowntree and his colleagues has dealt especially with effects obtained by treating the parents, it is hoped that the extract will prove likewise to have an important direct influence. At any rate Asher has recently reported the discovery of a thymic extract that does directly promote development. Hence there may soon be available in such extracts a valuable medicament for use in cases of delayed development in children. Possibly the thymic principle, too, will lend itself to adsorption on charcoal and thus become available for oral use. As Dr. Rowntree is reporting the work of his group before another section, it would scarcely be gracious for me to develop this topic further.

Passing mention only may be made of recent studies of the parathyroid glands in relation to calcium metabolism and skeletal disorders. Overactivity of the parathyroid glands may give rise to a variety of symptoms, such as joint pains, weakness and polyuria. These manifestations are more common in adults but are occasionally seen also in children. The relationship of parathyroid deficiency to fretfulness and disorders of personality is in need of further study.

COMPLICATING FACTORS IN ENDOCRINE RESEARCH

So much then for orientation.[1] The endocrinologist finds himself almost overwhelmed by the shower of blessings that are falling on him. He is somewhat bewildered by the multitude of fascinating problems that are opening up before him. Among these the translation of the laboratory results into their clinical meanings is especially attractive. But much of this translating must be done by the physicians themselves; hence my chief mission is to utter a Macedonian call.

Even the older endocrinology, however, was far from its final fruition in the field of pediatrics. Possibly in considerable measure because puppies and kittens are not good laboratory animals, the endocrinology of infancy still remains an almost virgin field. Likewise most of the hormone relationships between mother and child require elucidation. How does the infant fare in the transition from maternal endocrine support to hormone autonomy? When does the transition take place? What could be done for a poorly developing infant by endocrine treatment of the mother? What are the indications for supplementing feeding formulas by the direct administration of hormones? Perhaps these problems should be attacked directly rather than through the experimental laboratories. If so, the cooperation of the pediatrician is essential.

There is one aspect of endocrinology, in any case, that necessarily falls on the pediatrician. Medicine is now in a transitional phase. The ineptitude of regarding a man as a mere peripatetic collection of interesting organs is becoming increasingly clear. The personality of their possessor is more important than his organs, no matter what fascinating pathologic condition or secretory versatility they may disclose. By and large, however, endocrinology still remains in the medical Dark Age of preoccupation with organs. There is exigent need for the study of hormones as factors in personality. This problem must be studied largely

1. Further details may be found in an excellent series of summarizing articles published in THE JOURNAL from Feb. 9 to Aug. 31, 1935, and in the current Yearbook of Neurology, Psychiatry and Endocrinology in the Practical Medicine Series.

on human subjects, and the most fruitful period at which the study can be made is in the developing years when personality is in the making. Although he may need specialized technical assistance, the pediatrician should almost necessarily play a leading rôle in such studies, and the endocrinologist would be delighted to have him assume primary responsibility.

As the pediatrician undertakes endocrine research, he encounters several complicating factors, some of which have as yet received perhaps too little attention at the hands of clinical endocrinologists.

The very logic of the situation with which the investigator is confronted is likely to be misapprehended. One is prone to look for simple causal sequences. The intrinsically complex nature of the phenomenology can be illustrated by data from elementary inorganic chemistry. If a pinch of table salt and one of potassium bromide are thrown into a glass of water every possible combination of the substances will at once appear—sodium chloride, sodium bromide, potassium chloride, potassium bromide, sodium ion, potassium ion, chlorine ion and bromine ion. When equilibrium is established, the concentration of each constituent of the solution is determined by the concentration of each of the others. Thus, each factor entering into the equation is simultaneously a cause and an effect. One is therefore dealing with a logic of complexes and not merely with a chain of sequences in which causes and effects stay nicely separated. The same is eminently true of the physiology and pathology of hormones—the hormones influence the internal milieu and the milieu influences the actions of the hormones.

A special phase of the complex relationships is that the endocrine organs are immediately interrelated. For example, depression of the anterior pituitary body changes not only the circulating titer of each of its hormones but also the titers of at least the thyroid gland, adrenal cortex and sex glands and perhaps the parathyroid and pancreatic hormones. These changes in turn react on the pituitary body as well as exert their primary effects on the physiologic processes generally. It is therefore practically impossible to distinguish cleancut, uniglandular factors, since complex equilibriums are always involved.

To the clinical endocrinologist the problem of diagnosis is of course of major importance. A few endocrinopathies so stamp themselves on the physique as to be recognized even by the tyro, but frank cases of this sort are the exception rather than the rule. Often the history is informative and a skilful physical examination will bring out important diagnostic points, but for the recognition of the more obscure endocrinopathies laboratory aid is indispensable. Presumably each glandular disorder induces a characteristic change in the metabolic picture (equilibrium), and a beginning has been made toward the recognition of these. Thus a combination of depressed basal metabolism, secondary anemia, slow pulse rate, reduced blood pressure, relatively scanty urine, increased blood cholesterol content and depressed urinary nitrogen content commonly signifies thyroid deficiency. A particular need in present-day endocrine research is the further study of the metabolic pictures produced by each glandular disorder. No doubt many intergradations of pictures must always be reckoned with, but at least it may be possible to recognize those of the outstanding primary glandular disorders. An elaborate research of the type suggested was interrupted by the recent untimely death of A. W. Rowe.

A beginning, too, has been made in the direct determination of the hormone content of the blood. A study of the theelin titer is of practical aid in the understanding of menstrual difficulties in girls. Less directly interpretable is the rate of output of theelin in the urine. Further development of assay methods for use in diagnosis would be a valuable contribution to clinical endocrinology.

Collip's recent report of the discovery of antihormones holds out promise of a far-reaching increase of diagnostic resources. If for each hormone there should prove to exist a protective antihormone, it should be possible to isolate these and set up direct systems of titration. It would be theoretically possible—and perhaps practicable—to determine for each individual his precise endocrine status.

This leads to the consideration of another intrinsic complexity of endocrinology. If antihormones actually exist, then any given endocrinopathy is susceptible of two explanations. Take hypothyroidism for example: it may be due, as has hitherto been supposed, to a low output of thyroxine or, on the other hand, to an excess production of antithyroid hormone. It is encouraging to recognize, however, that the two possibilities should lend themselves to relatively simple recognition by therapeutic test. If the thyroxine titer were low, the patient would respond sharply to medication in small doses; if the antihormone titer were high, the threshold of sensitivity to thyroxine would be correspondingly elevated. This is Collip's principle of inverse response.

Another variable in the endocrine equation is the tissue reactivity of the subject. In his studies of endocrine factors in heredity Stockard has been led to the conception that it is the degree of reactivity to the hormones rather than glandular efficiency that is inherited. Riddle has found that some species of doves react to only one-fifteenth as much of a pituitary preparation as is necessary to give a reaction in other strains. The occurrence of circumscribed areas of myxedema in patients showing clinical hyperthyroidism affords a particularly striking example of tissue variability. At the present time this factor seems to be of theoretical rather than practical interest, but, should exact methods of diagnosis by blood assay be developed, it will need to be taken into account and compensated for in determining dosages. Perhaps even now the principle has some meaning as explaining the mixture of symptoms of glandular hyperactivity and hypo-activity that are encountered when a patient is in a transition stage of glandular involution; e. g., in the later stages of acromegaly.

One cause of tissue refractoriness might be vitamin deficiency. In the absence of adequate supplies of vitamin D, parathyroid extract is ineffective, and this fact may conceivably illustrate a principle of wide applicability. The converse relationship may also hold. Hartman has found that vitamin assimilation is influenced by the amount of adrenal cortical hormone available to the organism. The same may be true of other hormones. The pediatrician seems to be in a favorable strategic position to investigate the hormone-vitamin relationships.

Having taken into account as best one can the various factors that might give rise to endocrine deficiency, actual or virtual, and having determined on the hormone indicated in any given case, the question of dosage arises. This must be determined empirically for each subject. The reaction threshold, as previously suggested, can vary widely from case to case. One of

my adult subjects reacts sharply and objectively to thyroid in dosage of one-third grain (0.02 Gm.) a day. Sleeper and I studied a schizophrenic patient who took 60 grains (4 Gm.) a day over a period of weeks and with only minimal effects.

The question of dosage is important not only because of the necessity of adjusting it to optimum efficiency but because of the danger of evoking the production of antihormone or, at least, tissue refractoriness. Lisser has reported a case of tetany in which the outcome was fatal because of the fact that the patient ultimately became unresponsive despite the use of enormous doses of parathyroid extract. Such refractoriness may have arisen because of the unphysiologic way in which the hormone reached the circulation. When several hours' supply is administered at once, a succession of feasts and famines is set up that is but a poor imitation of a smooth natural inflow—and that perhaps delicately regulated to the bodily need prevailing at any given time. It is rather probable in such cases that the periodic subjection of the body to excessive hormone influence sets up a protective outpouring of antihormone, and that a cumulative vicious circle is thus established. It would seem desirable, therefore, to incorporate hormone preparations that are to be given hypodermically in an oil menstruum or an emulsion so that absorption will take place more evenly than when aqueous solutions are used. As an immediately practical point, evidence has recently been offered that the total effect of a given amount of hormone is severalfold greater when given so as to promote slow absorption. Small doses frequently repeated are also more effective than large doses at longer intervals. The explanation is probably the same as in the case just discussed. Both on empirical and on theoretical grounds, then, the smallest dosage of a given preparation that will produce the desired effect should be used. As an empirical rule, also, the omission of medication for one week of each month seems to be more effective than continuous medication. Possibly the vacations permit the body to dispose of accumulated antihormone.

Another reason for concern about dosage is that some hormones—perhaps all—are diphasic in their influence. Thus, thyroid gives either anabolic or catabolic effects depending on the amount used. As Jellinek and I as well as others have shown, it promotes the formation of red blood cells in small or moderate doses but leads to secondary anemia if too vigorously administered. Other examples of reversal of effects with change of dosage could be cited, but further research is needed to determine to what extent the diphasic reaction is characteristic of hormones in general. It is not unlikely that the operation of this principle would account in numerous instances for discrepancies in the results reported from glandular therapy.

To round out the tale of difficulties, attention may be called to the fact that glandular imbalance gives a picture that is decidedly different from that of a compensated deficit or plethora of hormone. This is most clearly seen in the reaction to ovarian extirpation in middle aged patients or in the nervous tension of the menstrual period. The manifestations are due to ovarian deficiency, but that condition, when compensated, as in girlhood or old age, is benign. Merely to overcome a given glandular deficit by substitution therapy is in principle fairly easy, but to reestablish a delicate glandular balance presents a much more difficult problem. This principle comes into practical consideration when the pediatrician undertakes the hormone treatment of menstrual difficulties in girls. The cycle depends on a rather complex interaction of hormones, and each addition or subtraction disturbs the balance among them. Ideal therapeutic results can be expected only when the distortions of the normal formulas are recognized and individually corrected. Since the relationships vary from period to period during the cycle, a highly complex theoretical problem is thus presented. Practically, however, nature seems to be able to make out fairly well on a makeshift basis and, if a few of the major abnormalities are artificially corrected, to make the other adjustments spontaneously. Otherwise endocrine therapy would never offer better than a forlorn hope.

So much, then, for the outstanding theoretical and practical difficulties in endocrine research. The situation is and must remain complex. The difficulties have always existed—hence, no doubt, the slowness with which advancement in practical endocrinology has occurred. Perhaps the frank recognition of them would afford better technics for dealing with them and lead to an acceleration of progress.

In the last analysis no amount of knowledge of the physiology of the rat—or even the monkey—will in itself solve the pediatrician's problems. At best, only principles and "leads" can be derived from studies on the lower animals. The ultimate human problems must be solved in human terms. Hence the only hope for the final understanding of the endocrinology of infancy and childhood is in research conducted by the pediatricians themselves. The old adage is apposite: You can lead a horse to water but the deglutition must be voluntary. If this paper has served in any way to make the beverage seem more attractive, its purposes will have been served. Seriously, it seems imperative that the pediatricians as a group should become more vigorously concerned with the problems of endocrinology. In conclusion may I reiterate a hope that in the study of these problems the most important of all, the influence of the hormones on personality, will not escape judicious and critical attention.

SUMMARY

The thyroid gland, despite numerous recent observations on other glands, is still the one of most importance to the practical pediatrician. Minor degrees of thyroid deficiency as causes of disorders in childhood are of frequent occurrence.

The derivation of active substances from the anterior lobe of the hypophysis has given somatotropic, gonadotropic, mammotropic, thyrotropic and adrenotropic fractions, each of which presumably enters into the problems of the pediatrician. The influence of the pituitary body on carbohydrate, fat and water metabolism demands practical consideration. The relation of the adrenal cortical hormones to growth and lactation is of special pediatric interest, as is also the newer work on thymic extracts. The influence of hormone factors on the personality demands study.

Some of the difficulties of endocrine research are the complex nature of the relationships involved, the difficulties of diagnosis, the recently reported existence of antihormones, variations of tissue reactivity, the diphasic influence of individual hormones and the special effects of glandular imbalance.

The responsibility for the final solution of the endocrine problems of infancy and childhood devolves primarily on the pediatricians.

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A HEMOLYTIC BLOOD TRANSFUSION REACTION WITH OLIGURIA

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My purpose in this paper is to present a case in which recovery followed a hemolytic blood transfusion reaction with suppression of urine.

In 1931 Bordley [1] presented a review of the literature and a report of cases of hemolytic transfusion reactions with oliguria, and he added three more from the records of the Johns Hopkins Hospital. From the study of these seventeen cases, according to Bordley,[1] a clinical syndrome that is characteristic of the reaction may be outlined as follows: (*a*) Immediately after the transfusion there is a sharp febrile reaction, followed frequently by hemoglobinuria and invariably by suppression of urine; (*b*) there is an interval of several days during which there is symptomatic improvement but continued oliguria, and (*c*) after that interval the characteristic symptoms (agitation or drowsiness followed by uremia with convulsions and coma) develop rapidly and usually reach their peak eight days after the transfusion. Progressive uremia is the picture in the fatal cases, while profuse diuresis accompanies recovery.

The pathologic picture as described by Baker and Dodds [2] and Witts [3] and as discussed by Bordley [1] is one of central or nodular necrosis of the liver, pale edematous kidneys, with the collecting tubules filled with cellular débris (desquamated tubular epithelium plus red blood cells and lymphocytes) and degenerative changes in all tubular epithelium.

In the case reported here the clinical picture was typical of a hemolytic blood transfusion reaction with oliguria.

A Negro man, aged 42, was admitted to the Cincinnati General Hospital at 8:11 p. m., Jan. 20, 1935. Approximately one-half hour earlier he was cut on the right forearm with a razor. There was a profuse hemorrhage of the arterial type, and the patient was brought to the hospital by a friend who wrapped the bleeding arm in a towel. During transportation the patient lapsed into unconsciousness and did not react until his arrival in the receiving ward. Examination revealed a laceration 12 inches (30 cm.) long over the volar surface of the right forearm. The radial artery and numerous other smaller arteries were clamped, the arm was wrapped in sterile dressings, and shock treatment was instituted. The blood pressure was 80 systolic, 50 diastolic on admission; the patient's skin was cold and clammy, with profuse perspiration. Seven hundred cubic centimeters of a 5 per cent solution of dextrose was given intravenously with the patient in shock position, and external heat applied. Later the patient's blood pressure was found to be 50 systolic, so 500 cc. of a 5 per cent solution of dextrose with 32 mg. of acacia was given. The blood pressure rose to 95 systolic, 60 diastolic. The patient was moved to the ward at 11 p. m. The white blood cell count was 18,000; urine analysis showed a specific gravity of 1.016 and an alkaline reaction. The urine was straw colored and contained no albumin. The amount of sugar was recorded as 3 + after the administration of dextrose. The microscopic examination was negative. At midnight 500 cc. of a 5 per cent solution of dextrose with 32 mg. of acacia was again given intravenously because the blood pressure had dropped to 60 systolic, 40 diastolic. At the completion of the injection the blood pressure was 100 systolic, 60 diastolic. The patient complained of nausea but did not vomit.

At 1 a. m. the patient's blood was typed and cross-matched. His blood and that of the donor were both type IV. Cross-matching showed no agglutination at the end of one-half hour. At 1:45, 500 cc. of citrated blood with 300 cc. of physiologic solution of sodium chloride was given. The pulse rate throughout the transfusion was 88. The patient made no complaints and showed no signs of what might be interpreted as an immediate reaction.

The patient was sent to the operating room at 2:30 a. m. Under gas anesthesia the wound was thoroughly cleansed and the edges were excised. Examination revealed division of the radial artery and of a number of tendons, and partial division of the median nerve and transverse carpal ligament. The tendons and nerve were repaired with fine black silk, the subcutaneous tissue was sutured with interrupted catgut, and the skin closed with interrupted silk. The patient was returned to the ward in good condition.

At 9:30 a. m. the patient was taking fluids well with slight nausea. He vomited a small amount of greenish material; the temperature was 103 F. At 2:30 p. m. the general condition was much improved. The blood pressure was 110 systolic, 70 diastolic, temperature 101.4 F., pulse rate 112 and respirations 24. Tetanus antitoxin, 1,500 units was given subcutaneously.

On January 22 the patient urinated for the first time after the operation (forty-nine hours previously). The bladder had not been distended and there was no pain or tenderness in the costovertebral angles. Urinalysis showed 500 cc. of reddish black urine, 3 + albumin, occasional white blood cells, 4 or 5 red blood cells per high power field, an occasional granular cast and a 4 + benzidine reaction. Ammonium chloride, 30 grains (2 Gm.), three times a day was ordered. Fluids were to be forced.

On January 23 the patient did not urinate. He vomited without nausea 700 cc. Fluids taken by mouth amounted to 2,800 cc. The blood urea nitrogen was 80 mg. per hundred cubic centimeters. An intravenous injection of 800 cc. of physiologic solution of sodium chloride and 50 cc. of a 50 per cent solution of dextrose was given.

On January 24 the patient voided 500 cc. of urine. A cough developed and a small amount of blood streaked sputum was expectorated. A urine examination showed reddish brown urine, albumin 3 +, many red blood cells and occasional white cells. A blood count showed 9,900 white blood cells and 2,740,000 red blood cells. Fifty cubic centimeters of a 50 per cent solution of dextrose was given intravenously.

On January 25 the patient vomited 500 cc. of greenish material without being nauseated. There was an output of 175 cc. of reddish brown urine, which showed albumin 3 + and a 2+ benzidine reaction. There were an occasional granular cast and white blood cell. The blood urea nitrogen was 100 mg. per hundred cubic centimeters; carbon dioxide, 31 volumes per cent. The red blood cell count was 2,600,000. Roentgen examination of the chest was negative. Hot moist packs were applied to the lumbar region; 1,000 cc. of Fischer's solution was given intravenously with 100 cc. of physiologic solution of sodium chloride. This was followed in twenty minutes by a severe chill, which lasted for fifteen minutes. The blood pressure rose to 180 systolic, 90 diastolic. The temperature after the chill was 102 F.

January 26 the patient had no complaints. He vomited without being nauseated a total of 600 cc. The total urinary output was 75 cc. of amber urine with albumin 2 +, benzidine 0, many white blood cells and a few granular casts. He again expectorated a small amount of blood streaked sputum, which was negative for tubercle bacilli. The blood urea nitrogen was 115 mg. per hundred cubic centimeters; carbon dioxide, 30 volumes per cent. Eight hundred cubic centimeters of a 10 per cent solution of dextrose was given intravenously.

January 27 the patient appeared somewhat drowsy and vomited four times a total of 725 cc. of material, which showed a 3 + benzidine reaction. The total urinary output was 405 cc. The temperature was normal, having shown a gradual curve

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3. Witts, L. J.: A Note on Blood Transfusion, with an Account of a Fatal Reaction, Lancet **1**: 1297-1299 (June 22) 1929.

downward from the postoperative temperature of 103 F. The patient continued to have blood streaked sputum. The urine was amber with 2 + albumin. There were occasional granular casts. Five hundred cubic centimeters of a 10 per cent solution of dextrose and 400 cc. of a 5 per cent solution were given intravenously.

January 28 the patient was moderately stuporous but he responded well, had no complaints and breathed comfortably. There was moderate pitting edema of both legs to the thighs

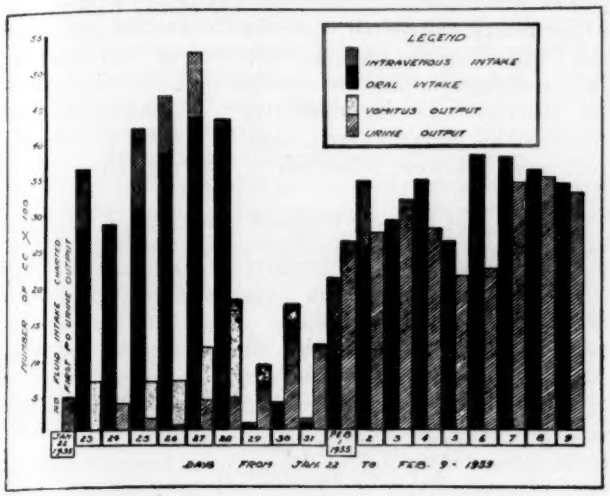

Chart 1.—Total daily fluid intake and output.

for the first time. There was a fluid wave in the abdomen and a moderate right hydrothorax. The ophthalmoscopic examination was negative. The patient vomited four times, a total of 1,275 cc., one specimen of which contained a moderate amount of bright red blood. He voided a total of 465 cc. of urine showing a specific gravity of 1.010, an acid reaction, 2 + albumin, clumped white blood cells, no casts, and a trace of benzidine. The blood urea nitrogen was 135 mg. per hundred cubic centimeters; carbon dioxide, 20 volumes per cent. The patient had had a total intake of approximately 30,000 cc. and a urinary output of approximately 2,200 cc. from the time of admission, with only slight edema of the legs. Fifty cubic centimeters of a 50 per cent solution of dextrose was given intravenously. The Karell diet replaced the regular diet. Sodium bicarbonate, 30 grains (2 Gm.), was given four times a day. The ammonium chloride was discontinued. The wound was dressed and part of the silk skin sutures was removed. The wound was well healed, with no evidence of infection or hematoma.

January 29 the patient was moderately stuporous but was rational and offered no complaints. He expectorated a small amount of blood streaked sputum and vomited 200 cc. of greenish fluid without blood. The urinary output was 660 cc., which showed a specific gravity of 1.015, light yellow color, alkaline reaction, no albumin, an occasional white blood cell, no blood by benzidine test and no casts. The patient's blood and blood from the donor were typed and cross-matched again. Both were type IV and the match was perfect at the end of eight hours. Fifty cubic centimeters of a 50 per cent solution of dextrose was given intravenously. The wound was healing well.

January 30 the patient offered no complaints. His general condition was unchanged. The edema of the legs had neither progressed nor receded. He vomited 200 cc. of greenish fluid (this was the last time that he vomited). The urinary output was 1,500 cc., and showed only a few white blood cells. The blood urea nitrogen was 110 mg. per hundred cubic centimeters; carbon dioxide, 17 volumes per cent. The patient had a rather severe nosebleed, which lasted for twenty minutes and was stopped by packing. Fifty cubic centimeters of a 50 per cent solution of dextrose was given intravenously.

January 31 the patient was free from edema; muscular twitchings were noted over the body and extremities. There was no increase in drowsiness. The urinary output was 1,200 cc. of normal urine. Fifty cubic centimeters of a 50 per cent solution of dextrose was given intravenously. The diet was changed from a Karell to a low protein salt-free diet with a fluid intake limited to 1,000 cc. daily.

February 1 there were no subjective complaints or objective changes. The urinary output was 2,600 cc. of normal urine. The blood urea nitrogen was 145 mg. per hundred cubic centimeters; carbon dioxide, 25 volumes per cent. Fifty cubic centimeters of a 50 per cent solution of dextrose and 1,000 cc. of Fischer's solution were given intravenously. The wound was completely healed.

February 2 all muscular twitching had ceased and there was no drowsiness. The patient wanted to get up and stated that he felt "fine." He voided 2,725 cc. of normal urine. The blood urea nitrogen was 165 mg. per hundred cubic centimeters and carbon dioxide was 28 volumes per cent. The blood count showed 1,000,000 erythrocytes. The patient's blood was typed and cross-matched for a transfusion. His blood and that of the donor were of type IV; they cross-matched perfectly at the end of one-half hour at room temperature, and no agglutination was noted after one hour in the incubator. He was given 50 cc. of a 50 per cent solution of dextrose intravenously. Six hundred cubic centimeters of citrated blood with 300 cc. of saline solution was given later with no immediate reaction.

February 3 there was no change in the condition. The patient voided 3,175 cc. of normal urine. Fifty cubic centimeters of a 50 per cent solution of dextrose was given intravenously.

February 4 the patient remained free from edema and made no subjective complaints. There was no drowsiness or muscular twitching. He voided 2,800 cc. of normal urine. Fifty cubic centimeters of a 50 per cent solution of dextrose was given intravenously.

February 5 there was no change noted. The patient voided 2,125 cc. of normal urine. The blood urea nitrogen was 135 mg. per hundred cubic centimeters; carbon dioxide, 43 volumes

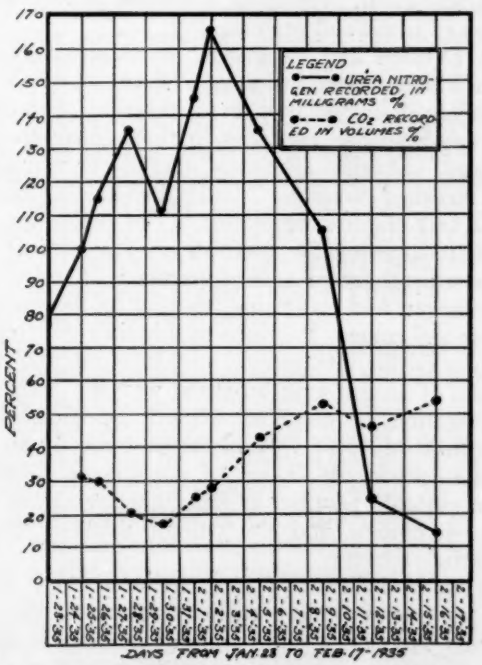

Chart 2.—Total daily urea nitrogen and carbon dioxide.

per cent. The red blood cell count was 3,400,000. Fifty cubic centimeters of a 50 per cent solution of dextrose was given intravenously.

From February 5, improvement was noted. February 9 the patient sat up in a chair without any apparent ill effect. The urine remained normal except for an occasional trace of albumin. The blood urea nitrogen was 105 mg. per hundred cubic centimeters; carbon dioxide, 53 volumes per cent. No special treatment had been given since February 5.

February 12 the patient had a small localized abscess over the left frontal area, and an elevation of temperature to 100 F.

The blood urea nitrogen was 24 mg. per hundred cubic centimeters; carbon dioxide, 46 volumes per cent. Hot saline solution compresses were applied to the abscess. The regular diet was given and fluids were taken as desired. Iron and ammonium citrate, 30 grains (2 Gm.), was given four times a day.

February 13 the left supra-orbital abscess was incised and drained. A phenolsulphonphthalein test showed a 35 per cent output in the first hour and 15 per cent in the second hour, a total of 50 per cent in two hours.

February 14 the patient was up and about with no complaints. Urinary concentration tests showed the following specific gravity values: at 7:45 p. m. 1.002, 9:45 1.004, 11:30 1.005, 3 a. m. 1.005, 5 1.005, 8:30 1.006, 10:30 1.008.

On February 15 the following specific gravity values were noted in the dilution test: at 9:10 1.007, 10:10 1,000, 11:10 1.001. These were the only adequate specimens obtainable.

February 16 the patient wanted to go home, said he felt well and had no complaints of any kind. The blood urea nitrogen was 14 mg. per hundred cubic centimeters; carbon dioxide, 54 volumes per cent.

February 18 the patient was discharged from the hospital with no subjective complaints or objective signs referable to the blood transfusion reaction. The last urinary specimen was clear and straw colored and showed an alkaline reaction, specific gravity 1.005, a trace of albumin, no sugar, an occasional white blood cell, no red blood cells, no casts and a negative benzidine reaction.

Since Bordley [1] reported his review of seventeen cases in 1931, Payne [4] has reported a typical case from Guy's Hospital in which the donor and the recipient were of type IV before transfusion. On a repeated cross-matching and typing after the transfusion they were found to belong to the type IV group and cross-matched perfectly. The patient died on the third day after transfusion, presenting a clinical picture of suppression of urine and uremia.

Von Deesten and Cosgrove [5] have also reported a case in which a transfusion of 750 cc. of whole blood was followed immediately by a reaction characterized by severe headache and pain in the lumbar spine and both legs. Shortly afterward there was vomiting of blood streaked vomitus. Later hematuria, hemoglobinuria and oliguria developed. The delayed reaction reached its peak on the ninth day. The clinical observations were those of severe uremia with retention of urea nitrogen and creatinine, rigidity of the neck, convulsions and coma. Previous to this time the treatment had included the intravenous and intramuscular administration of magnesium sulphate and the intravenous administration of dextrose without beneficial results. Venesection of 450 cc. of blood followed by an intravenous injection of 500 cc. of physiologic solution of sodium chloride resulted in immediate cessation of the uremic symptoms and the patient made a slow but uneventful recovery.

Johnson and Conway [6] have reported three cases in which there were typical reactions; Stewart,[7] two cases; Parr and Krischner [8] and Baron [9] have each reported one case, making an addition of ten cases to the literature since 1931.

4. Payne, R. V.: Acute Hemolytic Anemia: Death After Transfusion, Guy's Hosp. Rep. **84**: 65-71 (Jan.) 1934

5. Von Deesten, H. T., and Cosgrove, S. A.: Renal Insufficiency Following Blood Transfusion: Recovery After Venesection, Ann. Int. Med. **7**: 105-108 (July) 1933.

6. Johnson, R. A., and Conway, J. F.: Urinary Suppression and Uremia Following Transfusion of Blood, Am. J. Obst. & Gynec. **26**: 255-260 (Aug.) 1933.

7. Stewart, S. G.: Acute Renal Insufficiency Following Transfusion, M. Clin. North America **15**: 553-559 (Sept.) 1931.

8. Parr, L. W., and Krischner, Harald: Hemolytic Transfusion Fatality with Donor and Recipient in Same Blood Group, J. A. M. A. **98**: 47 (Jan. 2) 1932.

9. Baron, Charles: The Present Status of Hemolysis in Blood Transfusion with Report of a Fatal Case, Kentucky M. J. **30**: 326-328 (June) 1932.

A study of these twenty-nine cases, including the case reported in this paper, reveals the following: 1. The amount of blood given varied from 40 to 1,000 cc. 2. The citrate method was used thirteen times and whole blood ten times, the method not being specified in five instances. Once blood from the peritoneal cavity in a case of ruptured ectopic pregnancy was given. 3. There were eighteen deaths and eleven recoveries, a mortality rate of 62 per cent. 4. The peak of the reaction occurred from the third to the eighteenth day; excluding the patients who died at four and one-half and eight hours, the average time for the peak of the reaction was the ninth day. 5. Death followed transfusions varying from 230 to 1,000 cc., whereas recovery followed transfusions varying from 40 to 750 cc.

Polayes and Lederer [10] report a study of 2,500 blood transfusions and classify the causes of reactions as follows:

I. Incompatibility:
  (*a*) Errors in grouping.
    1. Poor technic.
    2. Use of low titered or contaminated serum.
    3. Weak agglutinins or agglutinogens in the recipient's blood.
    4. Pseudo-agglutination.
    5. Auto-agglutination, cold agglutination and subgroups.
    6. Anomalous or atypical agglutination.
    7. Contamination of recipient's blood by bacteria.
  (*b*) Indiscriminate use of the universal donor.
  (*c*) Immune iso-antibodies and hemolysins.
II. The use of unclean apparatus.
III. The use of citrate solutions.
IV. Incipient coagulative changes in the transfused blood.
V. Allergic phenomena in the recipient.
VI. Systemic diseases in the recipient.
VII. Transmission of disease to the recipient.

In order to place the present case in this classification, it must be classified as a reaction due to hemolysins in the recipient's blood, and thus it falls into the group of incompatibilities which cannot be forecast from the simple, direct cross-matching of the donor's and the recipient's blood.

This type of blood transfusion reaction is rare, as shown in the report by Witts [3] of a series of 3,430 blood transfusions without a single case of hemolytic reaction. It is a very serious reaction, as death has occurred in 62 per cent of all reported cases. In view of this fact one should consider the advisability of adding to the cross-matching procedure a test for hemolysis between the donor's and the recipient's blood.

SUMMARY AND CONCLUSIONS

1. A typical case of a hemolytic blood transfusion reaction with oliguria was studied, together with twenty-eight cases that have previously been reported.

2. The peak of the reaction after the transfusion usually occurs on the ninth day.

3. In the twenty-nine cases reported there were eighteen deaths, a mortality of 62 per cent.

4. Neither recovery nor death depends on the method of the transfusion or the amount of blood given.

5. The reaction appears to be one of hemolysis and cannot be forecast by cross-matching.

10. Polayes, S. H., and Lederer, Max: Reactions to Blood Transfusion, J. Lab. & Clin. Med. **17**: 1029-1043 (July) 1932.

ALLERGIC REACTIONS ASSOCIATED WITH COHABITATION

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The possibility of sensitization to emanations from individual human beings has been suggested in the past but, so far as we have been able to discover, no clearly authentic case of this type has been reported. Over quite a period of time, one of us included tests for sensitization to human hair in the routine sensitization studies. When, after several hundred such tests, it was found that no case had given a positive reaction, the use of this allergen was discontinued. One young woman with dermatitis from allergy to silk found that each time she had her hair trimmed the dermatitis over her neck and shoulders flared up. She was sensitive by scratch test neither to stock human hair nor to an extract of her own hair. A patch test with her own hair was negative. No special washes or other treatment of the hair was used at these times.

In the cases of supposed sensitization to human beings, it seems much more probable that some allergenic substance in the immediate environment of the person under suspicion is the etiologic agent. The following cases tend to confirm this premise:

CASE 1.—A woman, aged 38, perennially asthmatic, found that her asthma was increased when she slept with her husband. Among other things she was found sensitive to extract of tobacco smoke. Her husband was a heavy smoker. Following desensitization with tobacco smoke extract, her nocturnal asthma was decidedly improved. The patient was primarily intrinsically asthmatic, also sensitive to a number of extrinsic allergens, and, on the whole, relief from asthma was not satisfactory. At the same time, relief from the tobacco smoke factor at night was sufficiently marked to be convincing.

Other allergens may act in the same way in cohabitants. Thus, a young woman in our experience, sensitive to horse dander, had attacks of asthma whenever her brother went horseback riding and subsequently sat near her without first bathing and changing his clothes. Further possible applications of this type of exposure are obvious.

CASE 2.—A man, aged 30, who had had no previous allergic manifestations except an occasional attack of migraine, was married in the summer of 1934. About two months later a papular, pruritic dermatitis appeared on the legs, which soon involved both lower extremities and the lower part of the abdomen and back. The dermatitis became very extensive and was accompanied by considerable edema. The patient was found sensitive to wheat and silk. At first he stated that he did not have any direct contact with silk but later recalled that his wife wore a silk nightgown. She changed to linen night clothes and the patient left wheat out of his diet. The dermatitis was promptly relieved. After two weeks, when it had cleared up satisfactorily, his wife again wore a silk nightgown. The next morning he had a mild return of the dermatitis. Since then she has continued to wear linen and the dermatitis has not recurred, except on one occasion when he experimented with the eating of wheat.

CASE 3.—A man, aged 26, first seen in December 1933, suffered from a dermatitis involving both feet and ankles. He also gave a history of hay fever and was found sensitive to a number of pollens. Trichophyton was found in some of the scales from his feet and he was strongly sensitive to trichophyton extract. Among the foods he gave several positive reactions and he was placed on a diet. With dietary avoidances, local treatment and trichophyton desensitization the condition gradually cleared up, over a period of several months. When recovery was sufficiently advanced he experimented with additions of food to his diet and found that he could eat all positively reacting foods with impunity except lemon and chocolate. These he still avoids after fifteen months. When, occasionally, he inadvertently ingests one or the other of these, he has a return of the dermatitis.

The patient was married in the summer of 1934. For economic reasons it was felt that there should be some delay in the rearing of a family, and contraceptives were therefore employed. The first contraceptive used was a vaginal suppository with a base of oil of theobroma. Each time, within twenty-four hours after coitus, the patient experienced a disagreeable and embarrassing acute dermatitis of the genitalia. After a few weeks he recalled his sensitization to cocoa and, suspecting oil of theobroma as an etiologic factor, he changed the contraceptive to a contraceptive jelly. Since then he has had no return of these symptoms.

CASE 4.—A married man, aged 50, coming to the office in July 1934, complained of intense burning, stinging and itching of the shaft of the penis, which had started about six hours earlier, coming on about 4 o'clock in the morning. On examination the shaft and prepuce were swollen, edematous and very red, indicative of the acute inflammation present. When the patient was questioned, it was learned that he had had intercourse with his wife on retiring the night before and, as had been his custom for about twenty-five years, had used a condom. The patient then recalled that for the preceding two or three months he had had similar attacks of dermatitis on the penis, and for the first time he recalled that it always appeared after intercourse. A patch test was done with one of the condoms, which came out of the same box as the one he had used the night before. The patch test was applied to the inner side of the arm and another to the inner side of the thigh. Both of these patch tests, when removed twenty-four hours later, showed a good positive reaction. Since that time contraceptive jellies have been used and the patient has had no further trouble.

COMMENT

These cases illustrate the fact that symptoms associated with contact with some single individual are probably due to some allergenic substance in the person's immediate environment. In view of present immunologic concepts, this seems much more logical than some curious and unexplained sensitization to what are essentially homologous proteins. A few similar cases have been reported:

Rattner and Pusey[1] report the case of a young married man with dermatitis due to a certain perfume which his wife was in the habit of using.

Ford[2] reports a case of contact dermatitis due to quinine, confirmed by a patch test positive to the drug, and manifested by a vesicular dermatitis of the face, scalp and neck following two applications of Kreml Hair Tonic. Several months later this patient returned with a similar dermatitis involving the penis, scrotum, eyes, cheeks, ears and sides of the neck. It first started on the genitalia. This time the etiologic agent was found to be a contraceptive vaginal suppository containing quinine bisulphate and boric acid in a base of oil of theobroma.

Metzger[3] has described an interesting case of asthma from cohabitation. A sea captain was always free from asthma when on his vessel and on the high seas. Within half an hour or so after landing at port, any port, he would have a violent attack of asthma. The

1. Rattner, Herbert, and Pusey, W. A.: Neurodermatitis or Irritant Dermatitis? Report of Case, J. A. M. A. **99**: 1934 (Dec. 3) 1932.
2. Ford, W. K.: Drug Eruption Due to Quinine: Recurrence Following Use of Contraceptives, J. A. M. A. **103**: 483 (Aug. 18) 1934.
3. Metzger, F. C., Tampa, Fla.: Personal communication to the authors.

only substance to which he was found sensitive was orris root. The captain's "on-shore" proclivities may be easily deduced.

Duke[4] has described the case of a woman with asthma following coitus, which the husband thought due to sensitization to semen. Duke, however, concluded that it was a case of physical allergy due to heat and effort.

SUMMARY

So-called allergy to human beings can probably always be explained as due to some allergenic substance in the person's immediate environment. In some illustrative cases reported allergic reactions following concumbency or coitus have been explained in this manner.

Professional Building.

VARIABILITY IN THE STRENGTH OF TOXIN USED FOR THE DICK TEST

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AND
MAX M. GINSBURG, M.D.
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During the last two years we have encountered from time to time in the course of our work of immunization against scarlet fever, both by the hypodermic and by the intranasal method, reactions that appeared inconsistent and strikingly at variance with what had been anticipated. In our[1] publication on the subject we endeavored to account for such unexpected results by advancing the hypothesis that in some individuals the level of immunity to scarlet fever may vary from time to time, under the influence of factors beyond our knowledge. In the last six months the conviction has been forced on us that other factors play a part in the causation of these unexpected reactions. The experiences that led to this conclusion deserve, we believe, to be set forth in detail.

During November and December of 1934 we obtained from the use of one particular batch of Squibb's Dick Toxin uniformly strong positive reactions, and it was noted that almost every applicant for active immunization developed a positive reaction. The test was applied to a number of individuals who had had scarlet fever and it was most disconcerting to find that these too, in a large percentage of instances, yielded a positive outcome. Our colleagues using the same brand of toxin reported similar experiences. We communicated our difficulties to the manufacturers of this product and were informed that investigation showed this particular toxin to conform to established standards of potency. Needless to say that all tests had been performed with meticulous regard for every detail.

Despite the assurance of the manufacturers, we were convinced that this particular toxin was many times more potent than the Dick toxin we had used on previous occasions.[2] Our confidence in the reliability of the Dick test as an index to scarlet fever immunity had been shaken somewhat. Nevertheless, we felt quite certain, and are as fully convinced today, on the basis of personal experience and review of the literature, that the Dick reaction is, in the main, a dependable indicator of scarlet fever immunity and that successful immunization in positive reactors can be achieved by means of the injection or nasal insufflation of sufficient amounts of the specific scarlet fever toxin.

With the use of a new supply of toxin, our work progressed more satisfactorily for a time. However, we were destined to be disappointed again before long. On March 15, forty-one positive reactors at the Preventorium of the National Jewish Hospital received their initial inoculation of scarlet fever toxin by the hypodermic route. Successive weekly injections were given in accordance with the directions of the Dicks. On May 10, thirty-eight of these children were available for retesting, and twenty-three, or 60.5 per cent, gave a negative reaction. On May 11 the fifteen children who were still positive received a sixth injection of 80,000 skin test doses. On June 8, thirteen of these fifteen presented themselves for Dick testing. To our surprise, all thirteen were again positive; and what was even more disconcerting was to find the reactions in most instances of considerably greater intensity than the initial reactions. Moreover, the reactions persisted for from seventy-two to ninety-six hours. Mulford's products were used both for inoculation and for Dick testing. However, the toxin used for the final Dick test was purchased at a later date than the toxin used for the preliminary and second tests.

The following day, June 9, the very same toxin which produced these marked reactions was used in testing seven children who had shown a negative reaction on February 7. Two of these seven now presented a positive Dick. On the same day a second group of seven children who were positive on February 7 and had received five injections of toxin and had given negative reactions on May 10 were likewise retested with the same potent toxin. Four now showed positive reactions.

These results left no room for doubt that this particular toxin possessed a much higher degree of potency than that used in February and March. Thus, for the second time we came across a toxin that unmistakably failed to conform with established standards for potency.

In order to confirm this impression, we selected five children who were still positive (June 9) with this inordinately powerful Dick toxin of Mulford after having received six immunizing doses of toxin, and tested them on June 10 with a Squibb preparation which we had been using for some weeks in our office. Three of these were now negative, and two yielded mildly positive reactions. As a further check, twelve of the children inoculated with six doses of toxin and still positive with Mulford's were again tested with a newly purchased Squibb toxin. Only one of these twelve children showed a positive reaction.

In other words, the same group of children tested within a period of a few days with Dick toxin obtained from three different sources yielded results that varied within wide limits. This justifies the conclusion that Dick toxin designed to test the susceptibility of individuals to scarlet fever, and to determine the effectiveness of active immunization against this disease, possesses at times varying degrees of potency, and its use may lead to erroneous conclusions.

We were curious to determine whether the application of this inordinately powerful toxin of Mulford would yield an equally high incidence of positive reactions in another group of children. We could see no

4. Duke, W. W.: Clinic before the Virginia Carolina Tri-State Medical Association, Greenville, S. C., February 1933.

1. Friedman, Emanuel; Esserman, A. L., and Black, M. H.: Active Immunization Against Scarlet Fever by the Nasal Route, J. Pediat. 5: 504 (Oct.) 1934.

2. Of sixteen children who were negative with three different makes of Dick toxin, twelve yielded (June 28, 1935) strong positive reactions with this preparation.

reason for a different outcome. Accordingly, on June 28 we tested nineteen children free from acute infections, in residence at the Children's Hospital. The Mulford toxin bore the same serial number and expiration date as the one that gave rise to the strong reactions at the preventorium. As controls, we elected to use Squibb's and Parke, Davis's Dick toxin. To our utter amazement the reactions obtained from the application of these three different toxins were almost identical. Fifteen were negative to all three tests; four were positive to all three, with almost no variation in the degree of intensity; and in one instance Squibb's yielded a borderline positive, whereas the two other toxins proved negative.

This indeed was an unexpected outcome. If the Mulford toxin used at the Children's Hospital possessed—as it should—the same high potency as the product bearing the identical serial number and expiration date used at the preventorium, why did we not get a higher percentage of positives with the Mulford preparation than with the controls—as was the case at the latter institution? Are we not justified in our belief that the two products which should have possessed the same degree of potency were actually quite dissimilar in this respect?

These experiences make the conclusion inescapable that the Dick toxin manufactured by various pharmaceutical concerns lacks uniformity of composition. (Parenthetically, it may not be out of order to ask whether the toxin furnished for the active immunization against scarlet fever may not likewise vary in potency.) This doubtless constitutes a serious hindrance to the widespread practice of active immunization against scarlet fever. It is incumbent on the biologic houses to correct this unfortunate situation speedily and thereby pave the way for a more general acceptance by the profession of an effective prophylactic measure against a dreaded disease.

Furthermore, attention should be directed to the fact that in our limited experience approximately 12 per cent of a group of children reacted to the intradermal introduction of 0.1 cc. of phenol in the dilution of 0.4 per cent. This is the amount of phenol added to the Dick material as a preservative. Hence the advisability of controlling the Dick test by means of the injection of phenol in the concentration mentioned in order to eliminate false positive reactions.

And, again, it is quite likely that a certain percentage of positive Dick reactors owe their reaction to the protein substances found in the medium on which the streptococci has been grown, rather than to the specific toxin. This medium should therefore be made available so that we may be able to differentiate these protein reactions from those actually due to the specific toxin.

CONCLUSION

There is too great a variability in potency of the Dick toxin available at present, to make it serve as a dependable index to the presence or absence of immunity to scarlet fever.

Until this toxin is properly standardized and all commercial toxins are of uniform strength, it is impossible to determine with any degree of accuracy to what extent attempts at active immunization have been successful.

It would appear, therefore, that the present scheme of active immunization against scarlet fever rests on an insecure foundation.

326 Republic Building.

Clinical Notes, Suggestions and New Instruments

WHEAT HAIRS AND DUST AS A COMMON CAUSE OF ASTHMA AMONG WORKERS IN WHEAT FLOUR MILLS

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In the study of four consecutive cases of asthma observed among workers in wheat flour mills, I have been able to trace the source of illness, I believe, to sensitization to wheat hairs or the surface scales of wheat, or both. I believe that wheat hair is probably the morphologic structure which is responsible for a majority of cases of wheat asthma among millers.

The four patients all gave a like history of finding that they were subject to asthma while working in wheat mills, especially on windy days and when they worked in certain rooms in which they were exposed to the dust that came from the first cleaning of the wheat grain. The most severe attacks followed mishaps

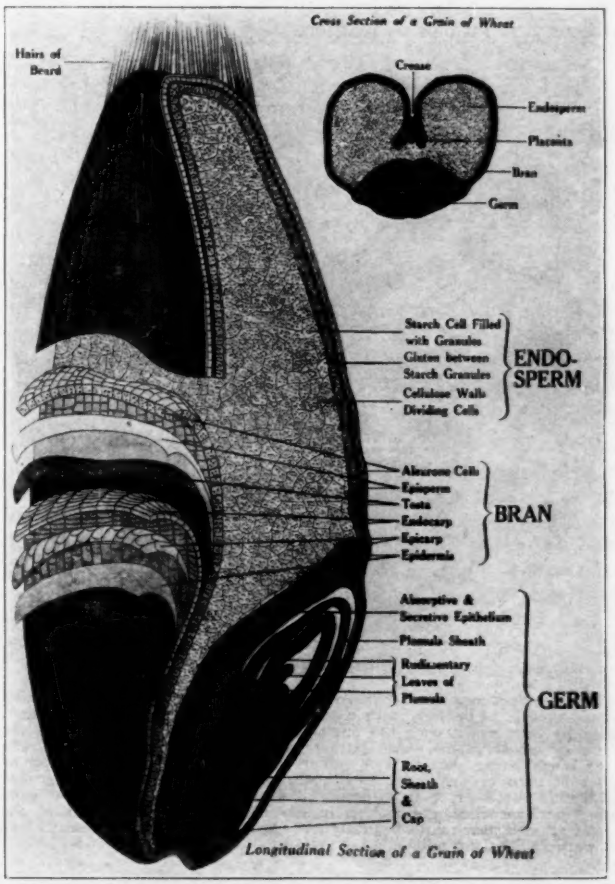

Fig. 1.—Longitudinal and cross section of a grain of wheat. Note sharp pointed hairs at the top of the longitudinal section, which are broken off at the first cleaning of the wheat grain. In the original from which this reproduction was made, the longitudinal section was magnified 70 diameters and the cross section 30.

in the machinery of the mill or the cleaning of apparatus or rooms that exposed the workers to unusually large amounts of this dust. Depending on the degree and duration of exposure, attacks of asthma would follow, which would last from a day to a week or more and vary from cough or marked asthma to a completely prostrating asthma that was difficult to relieve by therapeutic measures.

Apparently sensitization came on after several years' work in a mill and gradually increased in severity until it resulted, in two cases, in an illness that caused the patients to quit milling in spite of treatment with extract from wheat hairs and dust, which reduced the frequency and severity of their attacks. One patient was so disabled at the age of 53 by a complicating

emphysema that he was granted disability insurance. This patient was not grossly affected by any agent other than wheat dust.

The patients were all tested with extracts of the different fractions of wheat obtained in the process of milling; namely, dust obtained from the first polishing of wheat, from bran and germ, from the different grades of flour, from the dust obtained from the different localities in the mill, and from wheat rust.

Whereas reactions varying from a simple erythema to small wheals with small pseudopods and erythema were obtained with one or several of the fractions used, the gross reactions in every case were obtained first from extracts made up from dust escaping from the apparatus for the first cleaning of the grain and secondly from floor dust collected from localities in which this type of wheat dust was most abundant. The latter dust appeared macroscopically to be made up entirely of wheat flour. The former appeared microscopically to be made up of about equal quantities of hairs and the surface scales from wheat. It was difficult to separate these two elements, so that tests were made from the mixture of the two. Scratch tests made with the bran and germ fractions gave much smaller reactions than tests with hairs, and tests with the better grades of flour gave little or no reaction.

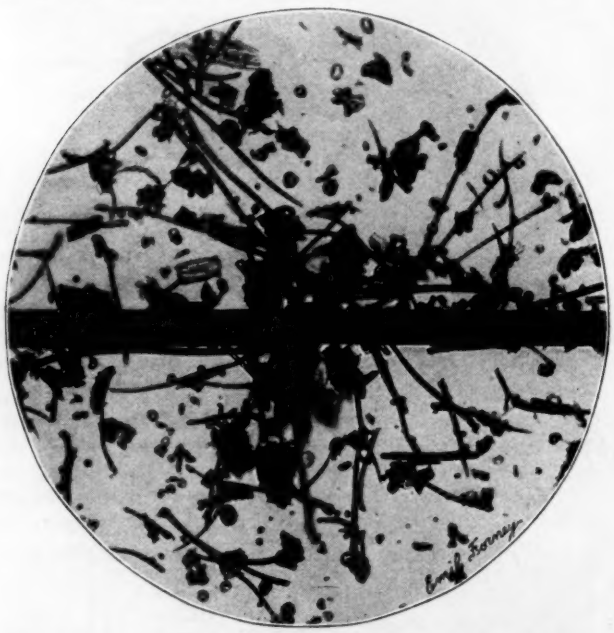

Fig. 2.—Specimen of dust taken from the first cleaning of wheat grains in the process of milling, with a human hair placed laterally in the dust. Note by comparison with the human hair how small and sharp are the hairs of wheat grains. An extract of this fraction of the grain gave very much larger skin tests in millers with asthma than did extracts of other portions of the grain, such as bran, germ, and the various grades of flour. Injection of infinitesimal amounts of wheat hair extract gave large local reactions and asthma in sensitive millers. The hairs of the wheat grain appear morphologically and chemically to be vicious sensitizers to workers in flour mills.

Intracutaneous tests with high dilutions of the hair and dust fractions would give rise to large wheals with pseudopods and large areas of erythema, and tests with high dilutions of extract given subcutaneously caused asthma.

TREATMENT

Two patients were treated with small ascending doses of wheat dust extract, with marked increase in their tolerance and gross symptomatic relief. However, after thorough trial these two patients became discouraged, in fact frightened into discontinuing their work as millers, because of severe attacks of asthma, which occasionally followed unavoidable gross exposure to the dust from wheat.

COMMENT

I once observed a case of iritis caused by hairs that had penetrated the cornea and lodged in the iris. These hairs could be seen with a corneal microscope and were the same color as the hairs in a brush used by the patient in applying remedies to the eye for conjunctivitis. The iritis was looked on as a foreign body reaction.

If one will observe the small size of wheat hairs as compared with human hair, shown in figure 2, one should be convinced that these hairs might penetrate delicate structures in the respiratory tract and no doubt cause foreign body reactions as well as sensitize susceptible individuals.

It is believed that the asthma observed in the millers is of two sources, one a foreign body reaction, the other an allergy reaction caused by sensitization to some substance contained in the wheat hair or carried into the tissues by the wheat hairs.

The cases of asthma referred to in this paper were unusually severe, prolonged and intractable. It is believed that this is due to the twofold source of asthmatic symptoms; namely, the foreign body reaction and the allergy reaction.

CONCLUSIONS

From experience gained from a study of four consecutive cases of asthma among wheat flour mill workers, sensitization to the hairs and outer cells of wheat proved to be the commonest cause of asthmatic symptoms.

Avoidance of wheat hairs gave relief in each case.

Continuous exposure to wheat hairs over a period of years caused debility and emphysema.

Treatment with extract of wheat hairs is partly successful but does not protect the patient against extreme exposure to wheat dust. A change in occupation is often advisable unless wheat dust can be avoided.

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PENTOSURIA IN TWINS

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This case is of interest for the following reasons: 1. It is the first recorded instance of pentosuria occurring in twins. 2. One of the twins is a physician. 3. Reducing substances in the urine have been known to be present for seventeen years. 4. The cases were previously reported as juvenile diabetes in twins [1] and as renal diabetes.[2]

History.—L. W., a man, aged 28, a physician, and M. W., his twin sister, came under observation in 1918, at the age of 11 years, because the girl complained of irritation of the genitalia and thirst. Examination of the urine revealed sugar at this time. Because the two children always suffered simultaneously from the same diseases, the mother had the boy's urine examined, and sugar was found in it also. Shortly thereafter the children were hospitalized for further study. The urine showed a reducing substance, which was analyzed and thought to be dextrose. The blood sugar of both children was 0.06 per cent. The diagnosis at this time was juvenile diabetes in twins. It was found that they were excreting from 1.5 to 3 Gm. of sugar daily, and this amount remained fairly constant, despite efforts to eliminate the sugar completely. After three months of dietary restriction the children rebelled and ate what they pleased, with the exception of sugar. The blood sugar was 0.08 per cent and there were no symptoms suggestive of diabetes. The children developed normally and two years later the mother reported that they were perfectly well, but the urine of both still contained sugar. The diagnosis at this time was renal diabetes.

In 1933 L. W. came to Montefiore Hospital as a member of the resident staff and, learning of our interest in the various urine sugars, he consulted us. The interval history was entirely uneventful; he and his sister had not adhered to any diet. Occasionally when troubled by his conscience or by the fear that true diabetes might develop he voluntarily omitted sweets, but a robust appetite soon reasserted itself. The urine always contained a trace of sugar, and the blood sugar was always within normal limits.

The reducing substance was found to be pentose. The sister's urine also contained pentose. Specimens from both parents and a brother were examined and found to be sugar free.

1. Strouse, Solomon: M. Clinics North America **1**: 1241 (March) 1918.
2. Strouse, Solomon: Renal Glycosuria, Arch. Int. Med. **26**: 768 (Dec.) 1920.

The reducing substance in the urine did not ferment with yeast and gave a positive Bial's test. Benedict's solution was reduced within ten minutes at 55 C.[3] On treatment with phenylhydrazine the characteristic pentosazone was formed. The melting point after purification was 160 C. Mixed with an equal quantity of *d*-xylosazone (prepared from *d*-xylose) and recrystallized from 95 per cent alcohol, the racemic xylosazone was formed and the melting point was elevated to 200 C. In this way the reducing substance was identified as *l*-xyloketose. In twenty-seven other cases of pentosuria that we have studied, the urine sugar has also been established as *l*-xyloketose.

COMMENT

Pentosuria and renal diabetes are similar in many respects and may easily be mistaken for each other. In both conditions sugar is found in all specimens of urine, and the blood sugar and sugar tolerance are normal. Neither condition produces symptoms, and the finding of sugar in the urine is often an accidental one. The diagnosis can be established only by chemical studies and identification of the reducing substance. By means of three simple tests it is possible to learn whether one is dealing with renal diabetes or pentosuria. In cases of renal diabetes the fermentation test is positive, Bial's test is negative and Benedict's solution is not reduced at 55 C. within ten minutes. In pentosuria the fermentation test is negative, Bial's test is positive and Benedict's solution is reduced at 55 C. within ten minutes, provided the urine pentose is *l*-xyloketose. If further identification is desired, the osazone should be prepared and identified by microscopic examination and determination of the melting point.

In our series we have encountered several cases that have been wrongly diagnosed as renal diabetes, and we would emphasize that in all cases of renal diabetes in which the reducing substance has not been identified another examination should be made, for it is in this group that one is most apt to discover cases of pentosuria.

Montefiore Hospital.

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2. Flinn, F. B.: Elimination of Radium Salts from the Human Body, J. A. M. A. **96:** 1763 (May 23) 1931.

PARATHYROID EXTRACT AND VIOSTEROL TREATMENT OF RADIUM POISONING

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In 1929 Flinn and Seidlin[1] reported the results of treating three cases of radium poisoning in painters of luminous dials by injections of parathyroid extract-Collip over a period of seven weeks. Their report was remarkable in that it showed a loss in radioactivity of about 50 per cent. In 1931 Flinn[2] reported an increase in the elimination of radium from the human body when the patients were given viosterol for some time. A marked decrease in radioactivity was again observed. The decrease in radioactivity was measured directly on the living subjects with an electroscope by the gamma method or by testing the radon present in the expired air of the patients.

Our patients were four radioactive girls of the New Jersey radium patients who were placed under the supervision of a commission consisting of Dr. James Ewing, Dr. E. B. Krumbhaar, and Dr. Lloyd F. Craver.

METHOD OF TREATMENT

The patients were not hospitalized but the administration of the drugs and the diet of the patients were carefully controlled. Since control over one of the patients was not so good as we desired, radium determinations were not made on her excreta.

The treatment was based on the assumption that the administration of a diet low in calcium together with injections of parathyroid extract might favor mobilization not only of calcium but also of part of the radium deposit in the bones, and possibly its excretion. Since these patients all showed rather pronounced structural changes in the bones, it was thought best not to continue this "radium and calcium mobilizing regimen" indefinitely but to provide rest periods of high calcium intake together with small doses of viosterol, which was believed to favor assimilation of calcium, in order to permit some repair. Accordingly it was decided to give periods of treatment as follows:

1. No treatment.
2. Three weeks of low calcium diet. Injections of parathyroid extract every other day, beginning with 10 units and increasing to 50 units a day.

Radium Elimination—Total Per Day Expressed in Micromicrograms (10^{-12} Gm.)

Period	Patient A	Patient B	Patient C
1. Nov. 3-6, 1930, no treatment	1,040	118	268
2. Nov. 24-27, 1930, low calcium diet + parathyroid extract	1,639	142	372
3. Dec. 15-18, 1930, high calcium diet + viosterol	895	190	375
4. Jan. 5-8, 1931, same as period 2	1,381	250	624*
5. Jan. 26-29, 1931, same as period 3	979	191	384

* This patient refused further injections of parathyroid extract.

3. Three weeks of high calcium diet, calcium lactate 20 grains (1.3 Gm.) three times a day, and viosterol from 5 to 10 drops three times a day.

4. Three weeks the same as period 2, the amount of parathyroid extract being increased to the maximum dose of 50 units more rapidly.

5. Three weeks the same as period 3.

Five collections of stools and urine were made, a three days collection of such excrement being lumped in separate containers.[3] The first collection was for three days preceding the beginning of the treatment. The four other collections were for the final three days of each treatment period, as enumerated.

RADIUM DETERMINATIONS

Each collection of feces was ashed and weighed. The radium determinations were made on aliquot parts of the residues, by the emanation method, the bisulphate fusion method[4] or solution in nitric acid[5] being employed. These determinations were all made in duplicate. The samples of urine were evaporated to dryness, ignited and weighed. One radium determination was made on each collection of urine. The radium content of the urine rarely exceeded 5 per cent of the total radium excreted.

The results of the radium determinations are given in very condensed form in the accompanying table.

In February 1929[6] patient A excreted a total of 1,115 micromicrograms ($1{,}115 \times 10^{-12}$ Gm.) radium per day; patient B, 322 micromicrograms.

In March 1931 Dr. Failla measured the radon expired by patient A. A decrease in activity of less than 10 per cent was observed.

In June 1932 a gamma ray measurement was made on patient A. The readings of the instrument came out practically the same as the value found in February 1929. Further examination of the patients for radioactivity following the experimental period was not found practicable.

COMMENT

The table clearly shows that the three patients responded only slightly to the administration of parathyroid extract with low calcium diet in their rate of elimination of radium, and the viosterol treatment with high calcium diet produced no increase. The increase observed for the parathyroid extract

3. Dr. W. D. Turner, Columbia University, in cooperation with the United States Radium Corporation, prepared the collection of excreta for the radium determinations. Dr. Henry C. Johnston of East Orange, N. J., supervised the details of medication and collection of excreta.

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5. Lind, S. C.: Practical Methods for the Determination of Radium, J. Indust. & Engin. Chem. **7:** 406, 1024-2029, 1915; **12:** 469, 1920.

6. Schlundt, Herman, and Failla, G.: The Normal Elimination of Radium, Am. J. Roentgenol. **26:** 265-271 (Aug.) 1931.

and low calcium intake, however, does not represent a substantial loss of radium. A simple computation will reveal this fact. If patient A eliminated radium at the increased rate of 1,640 micromicrograms daily for a period of three months, she would lose only 0.15 microgram of radium during this period. Since her radium content was about 20 micrograms, it will be noted that with her best record it would take a year and eight months to eliminate 1 microgram of radium, representing merely 5 per cent of the total radium in her system. Normally patient A eliminated about 3 per cent of the radium in her system in the period of a year and eight months. In other words, patient A, who had contracted radium poisoning fully eight years before, retained the radium tenaciously. The administration of neither parathyroid extract nor viosterol caused a substantial reduction in the total radium fixed in the system.

Central Park West at One Hundred and Sixth Street.

Special Article

THE RELATIONSHIP OF DRUG THERAPY TO AGRANULOCYTOSIS

CLINICAL LECTURE AT ATLANTIC CITY SESSION

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Since the disease agranulocytosis, or acute granulopenia, was first described in Germany [1] in 1922 and in the United States [2] in 1924 there has been much study concerning its pathogenicity and, in particular, its etiology. Since it was first described thirteen years ago there have been hundreds of reports of the disease in the medical literature and it was responsible for more than 1,500 deaths in the United States alone in the three year period ended in 1934.

There has been considerable discussion as to the occurrence of the disease before 1922, and this question is important because of the possible relation to various etiologic factors. It seems obvious that this disease is one that presents little diagnostic difficulty, since the clinical picture is dramatic, the outcome is usually fatal, and the physician who makes leukocyte counts should experience little difficulty in its recognition. It appears unlikely, therefore, that it occurred in any considerable numbers before the year 1922, for, if it had, expert clinicians of the preceding period would certainly have described it. Occasional instances of profound leukopenia, however, are recorded in the literature, such as the one reported by Brown [3] in 1902; but these were only rare and sporadic as compared with the prevalence of the disease today.

We [4] have pointed out in previous publications that the disease in the United States has occurred mainly in women of middle age, although no age is exempt, and that it occurs rarely in the colored race except in those instances in which a definite etiology, such as the administration of neoarsphenamine, can usually be established. Also we have called attention to the fact that it seems to be more prevalent in people of a better social status; and this is further indicated by its rarity in municipal and charity hospitals. When such cases do occur, the history of drug administration can usually be elicited. In addition, we have noted the prevalence of the disease among people of the medical group and our studies show its frequency in this group to be eight times that of the population of the United States at large.[4b]

Agranulocytosis seems to be world wide in its distribution and has been reported mainly from the so-called civilized countries. However, this might be explained on the basis of better facilities for diagnosis and reports. By far the largest number of cases apparently have occurred in the United States and Germany, while they have been fairly numerous in France and Italy but comparatively rare in Great Britain, where, according to Hall,[5] only twelve cases have been observed. It seems to occur in larger numbers in those countries which have become flooded with various synthetic drugs.

CHARACTERISTICS OF THE DISEASE

Agranulocytosis may be defined as a disease in which, essentially, there is a marked diminution, or total absence, of the granulocytes of the peripheral blood, which is followed by loss of cellular resistance and this, in turn, followed by infectious processes of various types. Although the basic pathologic change is a neutropenia of the peripheral blood, the underlying pathologic process in the bone marrow has not been completely worked out. It seems, however, that there is a hypoplasia of granulocytic elements in the bone marrow and it is our purpose in this paper to determine from available evidence whether or not these changes are caused by the use of certain drugs.

ETIOLOGY

Since the disease was first described, many efforts have been made to determine its cause. Among the first workers in this field were those who endeavored to establish a bacterial etiology, including Lovett,[2] working with Bacillus pyocyaneus, and, more recently, Dennis,[6] who attempted to show that the absorbed toxins from growing bacteria were capable of producing a profound leukopenia. Many efforts have been made to produce the disease in lower animals by the injection of any and all bacteria that have been isolated from the blood streams of various patients, but all of these have been generally unsuccessful and the degree of leukopenia produced by the injection of this class of products seems to be no different than that produced by the injection of any finely divided, inert, particulate matter.

Other theories of etiology have included one of dietary deficiency, as illustrated by the work of Langston and Day,[7] who have been able to produce marked leukopenia in monkeys by the use of diets deficient in vitamin G. However, their animals showed red cell and platelet deficiencies as well, resulting in a hematologic picture more nearly simulating aplastic anemia. Furthermore, Miller and Rhoads [8] have produced similar

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2. Lovett, B. R.: Agranulocytic Angina, J. A. M. A. **83**: 1498 (Nov. 8) 1924.
3. Brown, P. K.: A Fatal Case of Primary Acute Infectious Pharyngitis with Extreme Leukopenia, Am. Med. **3**: 649 (April 19) 1902.
4. Kracke, R. R., and Parker, F. P.: The Etiology of Granulopenia (Agranulocytosis), with Particular Reference to the Drugs Containing the Benzene Ring: (*a*) J. Lab. & Clin. Med. **19**: 799 (May) 1934; (*b*) Am. J. Clin. Path. **4**: 453 (Nov.) 1934.
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7. Langston, W. C., and Day, P.: Personal communication to the authors in May 1935.
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leukopenias with ulcerative stomatitis by feeding dogs a type of deficiency diet that causes black tongue. It is possible that these dietary deficiencies may play some rôle in the experimental production and clinical development of the leukopenic state.

Another conception of the cause of agranulocytosis is that which assumes a hormonic dysfunction and in support of this is the work of Britton and Corey,[9] who observed marked leukopenia in their groups of adrenalectomized cats. Also Thompson[10] has stressed the coincidental occurrence of menstruation in his cases of agranulocytosis and states that in eighteen young women with agranulocytic angina the onset of subjective symptoms occurred within a day or two of the onset of the regular menstrual period and that all were menstruating at the time of admission to the hospital. At first this appeared to be an important incrimination of hormonic disturbances in the production of the disease, but it was realized that young women with painful menstruation usually take various types of analgesics at that time, and this class of patients can now be explained on the basis of drug administration prior to and during the menstrual period. In this connection, Johnson[11] has reported the case of a doctor's wife who suffered recurrent attacks of agranulocytosis coincident with menstruation, which at first was thought to be etiologic in producing her attacks; but when she discontinued the use of cibalgine (containing amidopyrine), there were no further recurrences.

The experimental production and clinical development of various types of granulopenia, after contact with certain chemicals, has long been recognized. In 1910 Selling[12] made a careful study of three cases of profound leukopenia with hemorrhages that occurred as a result of the cumulative and delayed effect of industrial benzene poisoning, and since that time many observations have been made relative to the depressant action of benzene on the leukopoietic system; Weiskotten[13] has demonstrated the marked depressant effect of benzene on the hematopoietic system of rabbits and one of us[14] has shown that benzene can be injected into rabbits in such small quantities as to exert a selective action on the leukopoietic system, producing a profound leukopenia with the red cells and platelets unaffected. So far as is known at this time, benzene is the only chemical that will consistently produce a profound leukopenic state in an experimental animal.

RELATION OF DRUGS TO LEUKOPENIA

The first intimation that drugs might be responsible for agranulocytosis was a publication[15] in September 1931 describing a case of acute fulminant agranulocytosis following the ingestion of large quantities of acetphenetidin. Also in January 1932 it was reported[14] that eight of a series of nine patients had taken drugs of the coal-tar series prior to the clinical onset of their disease, and at that time unsuccessful efforts were reported to produce the disease in rabbits by the injection of amidopyrine, acetphenetidin, Peralga and Dial. In May 1933 Videbech[16] of Denmark reported a typical case following the administration of amidopyrine. This was followed by two cases reported by Costen,[17] one following amidopyrine and the other acetphenetidin. In 1933 deVries[18] reported from Holland one case following the administration of amidopyrine. These reports were then followed by that of Madison and Squier[19] in which they pointed out that all fourteen of their patients had developed the disease after the use of amidopyrine or one of its combinations. Following their report, Watkins[20] restudied the cases of agranulocytosis seen at the Mayo Clinic and found that thirteen of these had apparently followed the administration of amidopyrine. Then Holten, Nielsen and Transbøl[21] in Denmark reported that five cases of agranulocytosis had developed following amidopyrine medication while the patients were being hospitalized for other diseases. At the same time Jorgensen[22] reported another case from Denmark, after amidopyrine. There then followed rapidly an increasing number of reports of patients developing the disease following the use of amidopyrine particularly and involving some other drugs as well. These include one case by Andersen,[23] another by Holten, Nielsen and Transbøl,[24] fifteen by Seemann,[25] one by Larsen,[26] one by Randall,[27] fourteen by Hoffman, Butt and Hickey,[28] two by Zinninger,[29] four additional cases by us,[48] one by Zinberg, Katzenstein and Wice,[30] two by Rawls,[31] one by Benjamin and Biederman,[32] one following dinitrophenol by Bohn,[33] then eighteen by Groen and Gelderman[34] from Holland, two by Corelli[35] from Italy, one after dinitrophenol by Davidson and Shapiro,[36] seventeen by Fitzhugh,[37]

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six by Plum [38] from Denmark, one by Witt,[39] who also observed two others following amidopyrine, one by Knudsen [40] from Denmark, two following dinitrophenol by Dameshek and Gargill,[41] another after dinitrophenol by Silver,[42] seven by Jackson,[43] one by Johnson,[11] another by Holten, Nielsen and Transbøl,[44] one by Moltke [45] of Denmark, and then four from China by Zia and Forkner [46] in patients who were being treated for kala-azar with Neostibosan. Then Squier and Madison [47] reported six additional cases, one presumably following acetanilid, and this was followed by one from England by Fisher,[48] another English case by Smith,[49] one by Stone and Margolis,[50] then one from England by Hall,[5] and in the meantime Sturgis [51] had found that seven of the nine cases seen at the University of Michigan had followed the administration of amidopyrine. Then an additional one was reported by Plum [52] from Denmark, followed by one by Maarsso [53] of the same country. Finally, another after amidopyrine was reported by Taussig [54] and another by Limarzi and Murphy [55] in May 1935. This long list of reported cases of agranulocytosis apparently following the administration of drugs may not be entirely complete, but we find no reference to any others in the literature available to us.

Thus there have been reported at this time 172 cases of agranulocytosis that apparently have followed the administration of drugs. Of this group 153 followed the use of amidopyrine, six dinitrophenol, four Neostibosan, three acetphenetidin, two acetanilid, two antipyrine, one acetylsalicylic acid and one quinine. It can be readily seen, therefore, that the chief indictment of drugs in the production of this disease is against amidopyrine, either alone or in combination with one of the barbiturates, and it appears that there can be little question that amidopyrine is causative in a large number of cases. It also seems that the evidence incriminating dinitrophenol is quite definite. It is questionable as to whether acetanilid, acetphenetidin, antipyrine, acetylsalicylic acid and quinine are capable of producing the disease.

It has long been recognized that organic arsenical compounds are capable of producing profound leukocytic depression and, in some instances, complete bone marrow aplasia, and there are many reports of agranulocytosis following the administration of neoarsphenamine, such as those by Cassoute, Poinso, Zuccoli, Montus and Gueirard [56] and by Pouzin-Malegue.[57] Also it has been shown by Mink and Campbell,[58] in a careful study of reactions following the administration of neoarsphenamine in the United States Navy over a period of five years, that definite bone marrow depression occurs in a small percentage of the cases, with leukopenia being a predominant part of the hematologic picture. It should be pointed out here that the organic arsenical products are composed mainly of a double benzene ring structure.

Also there have been reported numerous instances of agranulocytosis and the granulopenic syndromes following the injection of the gold salts, which are widely used in the treatment of tuberculosis and arthritis in France. At least twelve of these have been reported by Lande,[59] Jacob and Douady,[60] Achard, Coste and Cahen,[61] Jacquelin and Allanic,[62] Braillon,[63] Angeras and Ginsbourg,[64] Chabaud, Ginsbourg and Langlet,[65] Flandin, Escalier, Sassier and Joly,[66] and Forestier.[67] Ten of the twelve patients were treated with crisalbine, which is a straight chain organic gold compound, while two were treated with solganol, which contains a benzene ring structure. It should be pointed out that all these patients were being treated for either tuberculosis or arthritis and apparently no effort was made to ascertain whether or not there was coincidental administration of amidopyrine or some of its preparations. Forestier [67] states that the administration of these analgesic preparations could not be excluded in his two patients. Thus, in a summary of the cases of agranulocytosis reported as having followed the administration of drugs, it seems that at least four definite classes of drugs can be incriminated: amidopyrine, dinitrophenol, gold salts and organic arsenical compounds.

In addition to the large number of patients that apparently have developed the disease following the administration of drugs, much clinical experimental evidence has accumulated to indicate that drugs are causative in agranulocytosis. For example, Madison and Squier [19] gave a single dose of amidopyrine to each of two patients who had recovered from the disease and this was followed by a profound fall in the granulocytes, with a recurrent attack. They also gave a normal person a similar dose, with no change in the

38. Plum, P.: Experimental og sam aarseg til agranulocytose, Ugesk. f. læger **96:** 916 (Aug. 23) 1934.
39. Witt, W. H.: Agranulocytosis with Report of a Case, and with Special Reference to Certain Barbiturates as a Cause of the Disease, J. Tennessee M. A. **27:** 283 (Aug.) 1934.
40. Knudsen, O.: Et helbredt tilfaelde af agranulocytoses opetaaet efter en meget tille amidopyrindosis, Ugesk. f. læger **96:** 923 (Aug. 23) 1934.
41. Dameshek, William and Gargill, S. L.: Studies in Agranulocytosis: Report of Two Cases of Agranulocytosis Following the Use of Dinitrophenol, New England J. Med. **211:** 440 (Sept. 6) 1934.
42. Silver, Solomon: A New Danger in Dinitrophenol Therapy: Agranulocytosis with Fatal Outcome, J. A. M. A. **103:** 1058 (Oct. 6) 1934.
43. Jackson, H.: The Relation of Amidopyrine and Allied Drugs to the Etiology of Agranulocytic Angina, Am. J. M. Sc. **188:** 482 (Oct.) 1934.
44. Holten, C.; Nielsen, H. E., and Transbøl, K.: Et nyt nosocomial tilfælde af agranulocytose, Ugesk. f. læger **96:** 1162 (Oct. 25) 1934.
45. Moltke, Otto: Amidopyrin-agranulocytose og achylihyppighed, Ugesk. f. læger. **96:** 1160 (Oct. 25) 1934.
46. Zia, L. S., and Forkner, C. E.: The Syndrome of Acute Agranulocytosis and Its Occurrence as a Complication of Kala-Azar, Am. J. M. Sc. **188:** 624 (Nov.) 1934.
47. Squier, T. L., and Madison, F. W.: Primary Granulocytopenia Due to Hypersensitivity to Amidopyrine, J. Allergy **6:** 9 (Nov.) 1934.
48. Fisher, J. H.: Agranulocytic Angina: Two Cases, Lancet **2:** 1217 (Dec. 1) 1934.
49. Smith, E. J.: Agranulocytic Angina Treated with Pentnucleotide, Lancet **2:** 1219 (Dec. 1) 1934.
50. Stone, C. H., and Margolis, Julius: Granulopenia Following Allonal, J. A. M. A. **103:** 1933 (Dec. 22) 1934.
51. Sturgis, C. C.: Tr. A. Am. Physicians, 1934.
52. Plum, P.: Agranulocytosis Due to Amidopyrine: An Experimental and Clinical Study of Seven New Cases, Lancet **1:** 14 (Jan. 5) 1935.
53. Maarsso, Christian: Et letalt forløbende tilfælde af agranulocytose efter amidopyrin (Klimaxid tabletter), Ugesk. f. læger **97:** 47 (Jan. 10) 1935.
54. Taussig, A. E.: Cutaneous Allergy Following the Ingestion of Amidopyrine, J. Allergy **6:** 291 (March) 1935.
55. Limarzi, L. R., and Murphy, I. G.: Amidopyrine and Granulopenia, J. Lab. & Clin. Med. **20:** 616 (March) 1935.
56. Cassoute, Poinso, Zuccoli, Montus and Gueirard: Agranulocytose pure après deux injections de novarsenobenzol: Syndrome cardiorénal transitoire; eosinophilie, Bull. et mém. Soc. méd. d. hôp. de Paris **48:** 14 (Jan. 8) 1932.
57. Pouzin-Malegue: A propos d'un cas d'agranulocytose post arsenobenzolique, Bull. et mém. Soc. méd. d. hôp. de Paris **52:** 1786 (Dec. 21) 1928.
58. Mink, O. J., and Campbell, H. D.: Toxic Effects of Arsenical Compounds Employed in the Treatment of Disease in the U. S. Navy, U. S. Nav. M. Bull. **31:** 383 (Oct.) 1933.
59. Lande, K.: Die günstige Beeinflussung schleichender Dauerinfekte durch Solganol, München. méd. Wchnschr. **74:** 1132 (July 8) 1927.
60. Jacob and Douady, D.: Un cas d'agranulocytose chez une tuberculeuse traitée par la crisalbine, Bull. et mém. Soc. méd. d. hôp. de Paris **54:** 798 (May 9) 1930.
61. Achard, C.: Coste, F., and Cahen, R.: A propos des désordres hématologiques provoqués par les sels d'or, Bull. et mém. Soc. méd. d. hôp. de Paris **48:** 547 (April 22) 1932.
62. Jacquelin, A., and Allanic, A.: Sur un nouveau cas d'agranulocytose post-chrysotherapie, Bull. et mém. Soc. méd. d. hôp. de Paris **48:** 539 (April 22) 1932.
63. Braillon, J.: Agranulocytose au cours de l'aurothérapie sans incidents, Le sang **8:** 352 (Feb. 5) 1934.
64. Angeras and Ginsbourg: Aleucie hémorrhagique (agranulocytose) post-chrysothérapie, Le sang **6:** 798 (June 1) 1932.
65. Chabaud, J.; Ginsbourg, B., and Langlet, L.: Un cas de syndrome agranulocytaire aurique fruste, Bull. et mém. Soc. méd. d. hôp. de Paris **49:** 1238 (Nov. 3) 1933.
66. Flandin, C.; Escalier, A.; Sassier, P., and Joly, F.: Un cas d'agranulocytose mortelle par intolerance à l'or chez un tuberculeuse pulmonaire, Bull. et mém. Soc. méd. d. hôp. de Paris **49:** 556 (April 28) 1933.
67. Forestier, J.: Rheumatoid Arthritis and Its Treatment by Gold Salts, J. Lab. & Clin. Med. **20:** 827 (May) 1935.

leukocyte count. Furthermore, the administration of amytal alone, a straight chain barbiturate, produced no effect on the blood counts of the patients who had recovered. Plum [52] studied the effect of a single dose of amidopyrine on a patient who had recovered from agranulocytosis, by giving only 3 grains (0.2 Gm.), this resulting in the leukocyte count falling from 9,000 to 1,900 in one and a half hours, and at the end of twenty-four hours the count was 2,000 per cubic millimeter. He concluded that a small, single dose of the drug has a marked depressant effect on the white cell count. Sturgis [51] gave amidopyrine in doses varying from 5 to 15 grains (0.3 to 1 Gm.) to three patients who had recovered from the disease and this was followed by a profound reduction in the leukocyte count, but the administration of 5 grains of barbital had no effect. Benjamin and Biederman [32] gave 10 grains (0.65 Gm.) of amidopyrine to a patient who had recovered, producing a leukopenia of 1,000 per cubic millimeter, twenty-four hours later. The same patient was then given acetylsalicylic acid and a barbiturate with no effect. In the series of Rawls,[31] of 200 patients being treated for arthritis with amidopyrine, two developed neutropenia and one of these recovered by simply leaving off the drug, but when it was resumed, a second attack was precipitated. Zinberg, Katzenstein and Wice [30] gave 5 grains of amidopyrine to a patient who had recovered, which was followed by a leukopenia of 2,700. Two weeks later the same patient was given another dose of 5 grains with a resulting leukopenia of 1,300. Therefore it can readily be seen from such experiments as these that certain individuals, especially those who have recovered from an attack of the disease, seem to be unusually susceptible to the action of the drug, to such an extent that successive attacks may be produced at will, but that this cannot be done in a person who is not susceptible. It does not necessarily follow that all cases of agranulocytosis would react in this way, as indicated by the observation of Limarzi and Murphy,[55] who treated a patient with a large quantity of amidopyrine, apparently followed by no ill effects. Terry and Sanders [68] have even treated a patient with myeloid leukemia by daily administration of amidopyrine and reported a reduction of the leukocyte count from 180,000 to 20,000 per cubic millimeter, although previous radiation therapy might have been responsible for this.

When the relationship of drug administration to agranulocytosis was first suspected, there soon followed attempts on the part of many investigators to reproduce the disease in lower animals by the administration of the drugs in question. One of us [14] reported the injection of rabbits with amidopyrine, acetphenetidin, Peralga and Dial, but with no effect on the leukocyte count in any of the animals. Madison and Squier [19] administered amidopyrine in large doses to rabbits by mouth and produced a leukopenia on the thirtieth day in only one animal out of eighteen. Hoffman, Butt and Hickey [28] stated that they fed amidopyrine to a number of rabbits and that this was followed in a few weeks by a definite depression of the total white cell count. Feeling that the Neostibosan used in the treatment of kala-azar might have been responsible for their four cases of agranulocytosis, Zia and Forkner [46] gave animals large and repeated doses of the drug and stated that they could observe no significant changes in the blood picture.

In previous studies we [4a] have shown that when benzene is injected into rabbits the effect on the bone marrow is probably produced by one of the oxidation products, and we have found that marked leukopenia could be produced by catechol and quinone [4b] but that no depressant effect was observed from the other oxidation products. Also we have demonstrated that amidopyrine can be oxidized easily, in vitro, under

TABLE 1.—*A Chronological List of Reported Cases of Agranulocytosis Following the Use of Drugs* *

Author	Where Observed	Date of Publication	No. of Cases	Drug Involved
1. Kracke	United States	Sept. 1931	1	Acetphenetidin
2. Kracke	United States	Jan. 1932	6†	Amidopyrine
3. Videbech	Denmark	May 1933	1	Amidopyrine
4. Costen	United States	June 1933	2	Amidopyrine, 1 Acetphenetidin, 1
5. de Vries	Holland	Sept. 1933	1	Amidopyrine
6. Watkins	United States	Nov. 1933	13‡	Amidopyrine
7. Holten and others	Denmark	Feb. 1934	5	Amidopyrine
8. Jørgensen	Denmark	Feb. 1934	1	Amidopyrine
9. Madison and Squier	United States	Mar. 1934	14	Amidopyrine
10. Anderson	Denmark	Mar. 1934	1	Amidopyrine
11. Holten and others	Denmark	Mar. 1934	1	Amidopyrine
12. Seemann	Denmark	Mar. 1934	15‡	Amidopyrine
13. Larsen	Denmark	Mar. 1934	1	Amidopyrine
14. Randall	United States	April 1934	2	Amidopyrine
15. Hoffman and others	United States	April 1934	14‡	Amidopyrine, 13 Dinitrophenol, 1
16. Zinninger	United States	April 1934	2	Amidopyrine
17. Kracke and Parker	United States	May 1934	4†	Amidopyrine, 2 Acetanilid, 1 Acetphenetidin, 1
18. Zinberg and others	United States	June 1934	1	Amidopyrine
19. Rawls	United States	June 1934	2	Amidopyrine
20. Benjamin and Biederman	United States	July 1934	1	Amidopyrine
21. Bohn	United States	July 1934	1	Dinitrophenol
22. Groen and Gelderman	Holland	July 1934	18	Amidopyrine, 14 Antipyrine, 2 Acetylsalicylic acid, 1 Quinine, 1
23. Corelli	Italy	Aug. 1934	2	Amidopyrine
24. Davidson and Shapiro	United States	Aug. 1934	1	Dinitrophenol
25. Fitzhugh	United States	Aug. 1934	17‡	Amidopyrine
26. Plum	Denmark	Aug. 1934	6	Amidopyrine
27. Witt	United States	Aug. 1934	1	Amidopyrine
28. Knudsen	Denmark	Aug. 1934	1	Amidopyrine
29. Dameshek and Gargill	United States	Sept. 1934	2	Dinitrophenol
30. Silver	United States	Oct. 1934	1	Dinitrophenol
31. Jackson	United States	Oct. 1934	7‡	Amidopyrine
32. Johnson	United States	Oct. 1934	1	Amidopyrine
33. Holten and others	Denmark	Oct. 1934	1	Amidopyrine
34. Moltke	Denmark	Oct. 1934	1	Amidopyrine
35. Zia and Forkner	China	Nov. 1934	4	Neostibosan
36. Squier and Madison	United States	Nov. 1934	6†	Amidopyrine, 5 Acetanilid, 1
37. Fisher	England	Dec. 1934	1	Amidopyrine
38. Smith	England	Dec. 1934	1	Amidopyrine
39. Stone and Margolis	United States	Dec. 1934	1	Amidopyrine
40. Hall	England	Dec. 1934	1	Amidopyrine
41. Sturgis	United States	Dec. 1934	7‡	Amidopyrine
42. Plum	Denmark	Jan. 1935	1†	Amidopyrine
43. Maarsso	Denmark	Jan. 1935	1	Amidopyrine
44. Taussig	United States	Mar. 1935	1	Amidopyrine
45. Limarzi and Murphy	United States	Mar. 1935	1	Amidopyrine

* Cases reported to have followed the administration of gold salts are not included in the table, because of inadequate investigation of other drug therapy. Cases following organic arsenicals are not included in the table, because of previous acceptance of their hematopoietic depressant action.
† Because of previous report, figures refer only to new cases.
‡ Figure refers to amidopyrine cases in a reinvestigated group.

conditions simulating those in the gastro-intestinal tract, and that the resulting product contains catechol and quinone. Climenko,[69] working with rabbits, found that the injection of quinone, catechol, dinitrophenol, antipyrine and phenylhydrazine would prevent the response of leukocytosis that normally follows the administration of nucleic acid products. He concluded, therefore, that the activity of the bone marrow of these

68. Terry, M. C., and Sanders, A. O.: A Case of Myeloid Leukemia Treated with Luminal and Amidopyrine, Proc. Soc. Exper. Biol. & Med. **31**: 1154 (June) 1934.

69. Climenko, D. R.: Inhibition of Leukogenic Activity in the Rabbit by Certain Cyclic Compounds, Proc. Soc. Exper. Biol. & Med. **32**: 823 (March) 1935.

animals was inhibited by these chemicals. Miller [70] gave amidopyrine orally to a group of sixteen dogs and found that the drug exerted a toxic effect on the bone marrow, but apparently insufficient to produce depression of the circulating elements of the blood. It can be seen, therefore, that experimental leukopenia in animals can be produced occasionally by the oral administration of drugs, with moderate frequency with their oxidation products, and consistently with benzene. It seems probable that another factor is necessary in the development of agranulocytosis in either the animal or man, and this factor may be that which is referred to as hypersensitivity, susceptibility, allergy or idiosyncrasy.

THE MECHANISM OF DRUG ACTION

Allergic reactions to drugs have long been recognized, but descriptions of this phenomenon have not included bone marrow or blood cellular changes. Unger [71] states that the coal-tar series of drugs are more important than any others from the point of view of allergy. Taussig [54] has reported an instance in which the patient used amidopyrine for many years with impunity, but after abstaining from the drug for several months he had a single dose of 5 grains, and this was followed immediately by a severe attack of urticaria, angioneurotic edema, bronchial asthma and a mild granulopenia, which lasted for several days. Squier and Madison [47] were able to demonstrate skin sensitivity to amidopyrine by patch testing in two of three patients who had recovered. They believe that acute granulocytopenia can be produced by repeated administration of amidopyrine to persons who have developed an allergic hypersensitivity to that drug. Groen and Gelderman [34] believe that certain individuals have an increased susceptibility or an idiosyncrasy to amidopyrine. Randall [27] studied the allergic response in his patient by injecting amidopyrine and phenobarbital subcutaneously, but this was not followed by a local reaction or change in the leukocyte count. Benjamin and Biederman [32] found no evidence of the allergic state in their patient with studies by intracutaneous and patch test methods. Limarzi and Murphy [55] also did patch tests on their patient, with negative results. Reznikoff [72] states that, when one considers the enormous amount of amidopyrine consumed and the relatively few individuals affected with granulocytopenia, it is obvious that one is dealing with the question of sensitivity in certain patients rather than with the universal action of the drug. Vaughn [73] has pointed out that a leukopenia will usually be found after ingestion of food to which a patient is sensitive; but, on the other hand, he emphasizes that the leukopenia involves all white blood cells and is not a true granulopenia.

It can be seen, therefore, that sufficient evidence has not accumulated to justify the statement that the action of amidopyrine is a true allergic response. It appears more probable that other factors influencing the fate and disposal of drugs in the animal body have not been worked out sufficiently to explain why the occasional person has a damaged hematopoietic system from the use of drugs.

We have presented evidence in previous publications [4] to indicate that in certain individuals amidopyrine may undergo an atypical oxidation reaction and that certain of these oxidation products have a depressing effect on the bone marrow and are capable of producing granulopenia in rabbits. This action brings up the question as to what part of the amidopyrine structure is responsible for its depressant effect. Herz [74] attributes the action to the attached pyrazolon group, mainly because this structure is found only in amidopyrine, and also because of its chemical similarity to phenylhydrazine, which is a recognized erythropoietic depressant. Andersen [23] also believes that it is the pyrazolon group which is the harmful element and not the benzene nucleus. On the other hand, there is more evidence to indicate that the bone marrow depression is caused by those products containing the benzene ring in such a form that they lend themselves to easy oxidation, and we have pointed out before that the benzene ring with either the attached amine or nitro group fulfils this requirement. We consider the ease of oxidation of the drug to be the most important factor and we are cognizant of the fact that many other drugs, such as acetylsalicylic acid, contain the benzene ring; but they do not oxidize readily and therefore are relatively harmless from a hematologic point of view. Furthermore, the occurrence of a group of cases following the administration of dinitrophenol is strongly indicative that the pyrazolon ring plays no part in the production of this disease.

Assuming that these drugs are capable of producing agranulocytosis in susceptible individuals, the question arises as to how much of the drug is capable of producing an attack. There can be no answer to this question, since the case reports show that an attack may be precipitated in one person by the administration of a single small dose, whereas in another it appears to result from the administration of large quantities over a long period of time.

Watkins [20] reviewed a series of thirty-two patients with granulocytopenia who had been seen at the Mayo Clinic and found that twelve of these had taken amidopyrine before the clinical onset, that twelve others had taken only the barbiturates, and that in eight patients no drug had been used before the onset of the illness. This was the first, and practically the only report, incriminating the barbiturates and it would appear more likely that thorough and adequate histories could not be obtained on this group. There has been little evidence to justify the inclusion of the barbiturates among the drugs causing agranulocytosis.

It should be emphasized that it is practically impossible to obtain a reliable drug history on a patient who is dead, regardless of all statements of relatives, friends and physicians, concerning medication in that patient. Since the drug theory of etiology has become widespread, Fitzhugh [37] has reviewed a series of patients and his report indicates that only a small percentage in the group followed the use of amidopyrine; but a negative history of drug usage has little value. We have attempted to obtain information from patients, with absolute denial of their having taken amidopyrine drugs, and in one instance found that the patient unknowingly had been taking large quantities of amidopyrine in a patented preparation, and this was ascertained only after chemical analysis of the product. In another instance we had to search through thousands

70. Miller, D. K.: Histological Changes in the Bone Marrow of the Dog Following Amidopyrine Administration, Science **80:** 320 (Oct. 5) 1934.

71. Unger, L.: Drug Idiosyncrasy, J. Allergy **3:** 77 (Nov.) 1931.

72. The Relation of Amidopyrine and the Barbituric Acid Derivatives to Granulocytopenia, Special Report of Council on Pharmacy and Chemistry, American Medical Association, J. A. M. A. **102:** 2183 (June 30) 1934.

73. Vaughn, W. T.: Personal communication to the authors, Dec. 3, 1934.

74. Herz, L. F.: The Rôle of Amidopyrine in Granulocytopenia, with Special Reference to Its Chemical Structure, J. Lab. & Clin. Med. **20:** 33 (Oct.) 1934.

of old prescriptions in a drug store to establish the fact that the patient had been taking amidopyrine. Patient 1 in Plum's [38] series was a woman who denied taking amidopyrine or any of its compounds, the patient's physician also stating that it could be absolutely excluded, and it was only after the most thorough investigation that this history was found to be unreliable. Another patient in Plum's series stated that she absolutely had not taken any amidopyrine preparations. In this her physician also agreed, and it was only on examination of her medicine chest that amidopyrine preparations, which she had been using, were found. Zinninger [29] lived in the same house with and prescribed for her two aunts, who both died from agranulocytosis. After their death she was amazed to find many empty containers of amytal compound in their apartment. These examples illustrate the difficulty of procuring a reliable history in a living patient, and it should be emphasized that a negative drug history is often a worthless one. Therefore, any large series of cases reinvestigated for history of drug administration, such as those reported by Jackson,[43] Fitzhugh [37] and Watkins,[20] are relatively unreliable.

Furthermore, since 1922, amidopyrine has been so widely used in combination with other preparations, such as the barbiturates, and the resulting mixtures have been given such a wide variety of names, that it is practically impossible for either patient or physician to be aware of what drugs do or do not contain amidopyrine. A list of some of the proprietary preparations that did, or do now, contain amidopyrine is given in table 2.

TABLE 2.—*A Partial List of American Proprietary Preparations That Did or Do Contain Amidopyrine* *

Name of Drug	Manufacturer
Allonal	Hoffmann-La Roche, Inc.
Alphebin	Gane & Ingram, Inc.
Amarbital	A. W. Kretschmar, Inc.
Amidol	Flint, Eaton & Co.
Amido-Neonal	Abbott Laboratories
Amidonine	Pitman-Moore Company
Amidophen	Eli Lilly & Co.
Amidos	The National Drug Company
Amidotal Compound	William H. Rorer, Inc.
Amifeine	McNeil Laboratories, Inc.
Aminol	The Smith-Dorsey Company
Am-Phen-Al	G. S. Stoddard & Co., Inc.
Ampydin	National Aniline & Chemical Company, Inc.
Amytal Compound	Eli Lilly & Co.
Analgia	The William S. Merrell Company
Antabs	The William S. Merrell Company
Baramid	McNeil Laboratories, Inc.
Barb-Amid	Sutliff & Case Company, Inc.
Benzedo Compound	Abbott Laboratories
Cibalgine	Ciba Company, Inc.
Cinchopyrine	Abbott Laboratories
Compral	Winthrop Chemical Company, Inc.
Cronal	Cronal Company, Inc.
Dymen	Coland Laboratories
Dysco	Abbott Laboratories
Eu Med	The Oralee Company
Gardan	H. A. Metz Company
Gynalgos	John Wyeth & Brother, Inc.
Hexin	Hexin, Inc.
Ipral-Amidopyrine	E. R. Squibb & Sons
Kalms	Johnson & Johnson
Lumodrin	Winthrop Chemical Company, Inc.
Midol	General Drug Company
Mylin	Mifflin Chemical Corporation
Neonal Compound	Abbott Laboratories
Neurodyne	Chicago Pharmacal Company
Nod	Reader Drug Company
Optalidon	Sandoz Chemical Works
Peralga	Schering & Glatz, Inc.
Phenamidal	The Upjohn Company
Phen-Amidol	Carroll Dunham Smith Pharmacal Company
Phenopyrine	Cole Chemical Company, Inc.
Pyramidon	H. A. Metz Laboratories, Inc.
Pyraminal	H. A. Metz Laboratories, Inc.
Seeqit	Laboratories JAQ, Inc.
Yeast-Vite	Yeast-Vite (U. S. A.), Inc.

* List supplied by Council on Pharmacy and Chemistry, American Medical Association (May 1935). This list does not include many of the large group of "patent medicines" or secret formula remedies.

COMMENT AND RECOMMENDATIONS

At this time it seems well established that amidopyrine, dinitrophenol and possibly other closely related drugs are incriminated as etiologic agents in agranulocytosis. Evidence to this effect is found in the widespread introduction of these drugs coincident with the appearance of the disease, in the occurrence of 172 cases that have been reported as following the use of these drugs, in the occasional patient who has recovered only to develop successive attacks on the readministration of the drugs, in the occasional experimental animal that has developed the disease after the introduction of the drugs or some of their oxidation products, and finally in the prevalence of the disease in that class of people who are the largest users of these drugs.

This conception of the etiology has received general confirmation throughout the world, as indicated by the reports of Plum [52] from Denmark, Groen and Gelderman [34] from Holland, Corelli [35] from Italy, Smith,[49] Fisher [48] and Hall [5] from England, and those of Sturgis [51] and many others from the United States. Johns [75] states that he has seen ten cases of this disease, in all of which a history of drug administration could be elicited. Groen and Gelderman [34] conclude that a drug etiology of agranulocytosis is much more often the rule than the exception. Plum [52] states that since the etiologic significance of amidopyrine has become a subject of general discussion in Denmark no new patient with agranulocytosis has been admitted to the Blegdams Hospital during a five months period, whereas in the same five months in the preceding year five patients were seen with the disease. We are impressed with the decreased number of cases in Georgia since knowledge of this relationship of drugs has become widespread among physicians and the public.

The question now arises as to what should be the attitude of the physician with respect to these drugs, particularly amidopyrine. The Council on Pharmacy and Chemistry of the American Medical Association,[72] in its recommendations concerning this question, discourages the indiscriminate administration of amidopyrine and, in particular, the exploitation of this drug to the public, in which individuals are urged to resort to self medication, and it condemns the situation whereby a potentially harmful drug is exploited to the public under a hundred different uninformative trade names. It seems desirable that it should be dispensed only by physicians in nonrefillable prescriptions, so that this danger of agranulocytosis may be largely removed from the unprotected public. Furthermore, it seems that every physician should prescribe amidopyrine with caution and he should not follow the careless custom of giving a patient a prescription for relief of pain with such indefinite direction as to have it refilled whenever the patient chooses to do so.

Amidopyrine is admittedly a valuable drug and, no doubt, has its place in therapeutics, but only under well controlled conditions and under supervision of a physician; and even then the leukocyte count should be checked from time to time to determine whether or not there is bone marrow depression.

A discussion of the relationship between drug administration and agranulocytosis would be incomplete without some comment relative to drug therapy after the disease has developed. It seems to us that the most valuable therapeutic measure that can be employed is to refrain carefully from using amidopyrine drugs dur-

75. Johns, F. M.: Personal communication to the authors, Dec. 17, 1934.

ing the attack, and it seems probable that the recovery of a patient is sometimes due to the mere omission of the offending drug, and it is in such instances that some supposedly remedial agent is often erroneously credited with a therapeutic efficacy that it does not deserve. If physicians would use these drugs with caution, if their indiscriminate sale could be controlled, and if the distribution of patented preparations containing amidopyrine could be suppressed, it is possible that this disease, which has now claimed thousands of lives, might entirely disappear.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

COD LIVER OIL CONCENTRATE LIQUID (LEDERLE).—A concentrate of the unsaponifiable fraction of cod liver oil dissolved in sufficient cod liver oil to give the desired potency to the marketed product. It has a vitamin A potency of not less than 55,100 units (U. S. P. X Revised, 1934) per gram and a vitamin D potency of not less than 5,510 units (U. S. P. X Revised, 1934) per gram.

Actions and Uses.—It possesses the therapeutic properties attributed to the vitamins present in cod liver oil.

Dosage.—For the concentrate in vials, 9 drops (3 minims, 0.18 cc.) daily for infants (the vials are marketed with a dropper designed to dispense three drops to the minim); for the capsules, one to two daily for children, two to three daily for adults.

Manufactured by the Lederle Laboratories, Inc., Pearl River, New York. No U. S. Patent or trademark.

Cod Liver Oil Concentrate Liquid (Lederle), Vials, 5 cc.—Each minim (3 drops, 0.06 cc.) has a vitamin A potency of not less than 3,138 units (U. S. P. X Revised, 1934) and a vitamin D potency of not less than 314 units (U. S. P. X Revised, 1934).

Cod Liver Oil Concentrate Liquid (Lederle) Capsules, 3 minims.—Each capsule has a vitamin A potency of 9,400 units (U. S. P. X Revised, 1934), and a vitamin D potency of 940 units (U. S. P. X Revised, 1934).

LAROCAINE HYDROCHLORIDE.—*p*-aminobenzoyl-2-2-dimethyl-3-diethylaminopropanol hydrochloride.—γ-diethylamino-β-β-dimethylpropyl-*p*-aminobenzoate hydrochloride.—$NH_2(C_6H_4CO)OCH_2C(CH_3)_2CH_2N(C_2H_5)_2.HCl$. The base of larocaine belongs to the procaine type. It differs from procaine in having a propanol group instead of the ethanol group and has two methyl groups attached to the former.

Action and Uses.—Larocaine hydrochloride acts as a surface as well as a conduction (infiltration) anesthetic and compares quite favorably in both fields with either cocaine or procaine. Larocaine hydrochloride is quick in action and produces anesthesia of a somewhat longer duration than cocaine or procaine. The average duration of conduction anesthesia is from three to five hours. Larocaine hydrochloride is non-narcotic and non-habit forming.

Dosage.—For corneal and conjunctival anesthesia, from 2 to 5 per cent solutions may be used. In otorhinolaryngology, 5 to 10 per cent solutions have been employed. From 0.75 to 1 per cent solutions are used in urology. For conduction anesthesia, 0.25 to 2 per cent solutions may be used. Solutions of larocaine hydrochloride may be sterilized by boiling for ten minutes. Epinephrine when desired may be added just prior to administration. Stock solutions should be kept in dark bottles. The product is supplied in vials containing ⅛, ¼, ½ and 1 ounce of larocaine hydrochloride in powder form.

Manufactured by F. Hoffmann-LaRoche & Co., Basle, Switzerland (Hoffmann-LaRoche, Inc., Nutley, N. J., distributor). U. S. patent 1,824,676 (Sept. 22, 1931; expires, 1948). U. S. trademark 283,775.

Larocaine hydrochloride occurs as a fine white, odorless, crystalline powder; when applied to the tongue, it possesses a bitter taste followed by a sense of numbness; permanent in the air at ordinary temperatures; freely soluble in water; soluble in alcohol; sparingly soluble in chloroform, insoluble in ether. Its aqueous solution is faintly acid to litmus. Larocaine hydrochloride melts at 196-197 C., with decomposition. From aqueous solutions, alkali carbonates and hydroxides precipitate the free base as a colorless oil, which solidifies after a time at ordinary temperature.

Dissolve about 0.05 Gm. of larocaine hydrochloride in 50 cc. of water; separate portions of 5 cc. each; to one portion add 5 cc. of silver nitrate solution: a white precipitate results, soluble in an excess of ammonia water; to another portion add 0.2 cc. of diluted hydrochloric acid, 0.2 cc. of a 10 per cent solution of sodium nitrite and gradually mix with a solution containing 0.2 Gm. of betanaphthol dissolved in 10 cc. of a 10 per cent sodium hydroxide solution: a red precipitate is formed (*distinction from the anesthetics not responding to the diazo reaction*); to another portion add 0.3 cc. of diluted sulphuric acid, followed by the addition of 0.5 cc. of tenth-normal potassium permanganate solution: the red coloration disappears immediately (*distinction from cocaine and some other local anesthetics*). Dissolve about 0.1 Gm. of larocaine hydrochloride in 1 cc. of sulphuric acid: the solution is colorless (*readily carbonizable substances*). Saturate about 0.1 Gm. of larocaine hydrochloride dissolved in 10 cc. of water with hydrogen sulphide: no coloration or precipitation results (*salts of heavy metals*).

Dry about 0.5 Gm. of larocaine hydrochloride, accurately weighed, at 100 C., for six hours: the loss in weight does not exceed 1 per cent. Incinerate about 0.5 Gm. of larocaine hydrochloride, accurately weighed: the residue is not more than 0.1 per cent. Transfer about 0.3 Gm. of larocaine hydrochloride, accurately weighed, to a 500 cc. Kjeldahl flask and determine the nitrogen content according to the official method described in Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists, third edition, page 20, chapter 2, paragraph 22: the percentage of nitrogen corresponds to not less than 8.8 per cent, nor more than 9 per cent when calculated to the dried substance. Transfer about 0.3 Gm. of larocaine hydrochloride, accurately weighed, to a suitable Squibb separatory funnel, add 25 cc. of water, followed by the addition of 5 cc. of ammonia water, extract with seven successive portions of ether using 35 cc., 30 cc., 25 cc., 25 cc., 20 cc., 15 cc. and 10 cc., respectively; wash the combined ethereal solution with 15 cc. of water, filter through a pledget of cotton and evaporate to a thick oil in a stream of warm air; expose over sulphuric acid in a partially exhausted desiccator; dissolve the oily residue in about 20 cc. of previously neutralized alcohol; warm slightly; add 12.5 cc. of tenth-normal hydrochloric acid solution, followed by the addition of an equal volume of water; determine the excess of acid by titration with tenth-normal sodium hydroxide solution, using methyl red as an indicator: the amount of tenth-normal hydrochloric acid solution consumed corresponds to not less than 87 per cent nor more than 89 per cent aminobenzoyldimethyldiethylamino propanol, when calculated to the dried substance. Transfer the ammoniacal aqueous portion from the immiscible solvent extraction to a 400 cc. beaker and place on the steam bath for three hours, add 100 cc. of water, followed by the addition of 10 cc. of nitric acid and 25 cc. of silver nitrate solution, subsequently boil, with continuous stirring, and allow to cool in a dark place. Collect the precipitate of silver chloride on a Gooch crucible, wash with a diluted nitric acid and water, followed by alcohol and ether; finally dry to constant weight at 105 C.: the amount of hydrogen chloride calculated from the silver chloride found corresponds to not less than 11.5 per cent nor more than 11.7 per cent when calculated to the dried substance.

WHITE'S COD LIVER OIL CONCENTRATE (LIQUID).—A concentrate of the unsaponifiable fraction of cod liver oil dissolved in sufficient cod liver oil to give the desired potency to the finished product. It has a vitamin A potency of not less than 60,000 units (U. S. P. X Revised, 1934) per gram and a vitamin D potency of not less than 8,500 units (U. S. P. X Revised, 1934) per gram.

Actions and Uses.—It possesses properties similar to those of cod liver oil so far as these depend on the vitamin content of the latter.

Dosage.—For the Liquid: Infants, from six to eight drops daily; children, two to four drops daily; adults, four drops three times daily. The liquid is marketed with a dropper designed to supply ⅔ minim (0.041 cc.) in each two drops. For the Capsules: Children, one capsule daily; adults, one to two capsules daily.

Manufactured by Health Products Corp., Newark, N. J. U. S. patent 1,984,858.

White's Cod Liver Oil Concentrate Capsules, 3 minims.—Each capsule contains White's Cod Liver Oil Concentrate (Liquid) 3 minims and has a vitamin A potency of not less than 10,260 units (U. S. P. X Revised, 1934) and a vitamin D potency of not less than 1,453 units (U. S. P. X Revised, 1934).

White's Cod's Liver Oil Concentrate Liquid, Vials, 50 cc.—Each ⅔ minim (0.038 Gm.) has a vitamin A potency of not less than 2,280 units (U. S. P. X Revised, 1934), and a vitamin D potency of not less than 323 units (U. S. P. X Revised, 1934).

DEXTROSE (See New and Nonofficial Remedies, 1935, p. 280).

Wm. S. Merrell Co., Cincinnati.

Ampoules Solution Dextrose 50%, 20 cc.: Each cubic centimeter contains approximately 0.57 Gm. of anhydrous dextrose.

Ampoules Solution Dextrose 50%, 50 cc: Each cubic centimeter contains approximately 0.57 Gm. of anhydrous dextrose.

DIPHTHERIA TOXOID (See New and Nonofficial Remedies, 1935, p. 392).

Parke, Davis & Co., Detroit.

Diphtheria Toxoid.—(See New and Nonofficial Remedies, 1935, p. 395). For determining sensitivity to the nonantigenic portion of diphtheria toxoid, a diluted diphtheria toxoid is supplied. This is marketed in packages of one 0.5 cc. vial and in packages of one 5 cc. vial containing diluted diphtheria toxoid sufficient for five and fifty reaction tests, respectively.

Committee on Foods

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COMMITTEE ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOLLOWING ANY NECESSARY CORRECTIONS OF THE LABELS AND ADVERTISING TO CONFORM TO THE RULES AND REGULATIONS. THESE PRODUCTS ARE APPROVED FOR ADVERTISING IN THE PUBLICATIONS OF THE AMERICAN MEDICAL ASSOCIATION, AND FOR GENERAL PROMULGATION TO THE PUBLIC. THEY WILL BE INCLUDED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED BY THE AMERICAN MEDICAL ASSOCIATION.

RAYMOND HERTWIG, Secretary.

SPINTRATE TABLETS (CANDY COATED)

Distributor.—M & R Dietetic Laboratories, Inc., Columbus, Ohio.

Manufacturer.—Spinach Products Company of South Carolina, Columbia, S. C.

Description.—Candy-coated powdered spinach tablets. The powdered spinach (Spintrate, THE JOURNAL, Aug. 5, 1933, p. 448) contains small quantities of agar, gelatin or acacia gum, and stearic acid. The candy coating is sugar colored with United States Department of Agriculture certified color.

Manufacture.—Powdered spinach is admixed with small quantities of agar, gelatin or acacia gum, and stearic acid to permit molding into tablets, which are coated with colored sugar. Each tablet contains 0.4 Gm. of powdered spinach and 0.2 Gm. of sugar coating.

Analysis (submitted by manufacturer).—

	per cent
Moisture	6.0
Ash	10.7
Fat (ether extract)	1.4
Protein (N × 6.25)	20.4
Crude fiber	5.5
Carbohydrates other than crude fiber (by difference)	56.0

	parts per million
Calcium (Ca)	7,100
Chlorine (Cl)	4,000
Copper (Cu)	6
Iron (Fe)	350
Magnesium (Mg)	2,800
Manganese (Mn)	90
Phosphorus (P)	4,200
Potassium (K)	29,300
Sodium (Na)	14,600
Sulphur (S)	2,700

	parts per billion
Iodine (I)	460

Calories.—3.2 per gram; 91 per ounce; 1.9 per tablet.

Vitamins.—Biologic assay shows Spintrate to be an excellent source of vitamins A, B and G.

Claims of Manufacturer.—Excellent source of iron and iodine.

JENNY LEE BRAND GENUINE EGG NOODLES
MINNESOTA BRAND EGG NOODLES—BROAD, FINE OR CHOW MEIN STYLE, MEDIUM WIDE

Manufacturer.—Minnesota Macaroni Company, St. Paul.

Description.—Egg noodles prepared from durum flour, egg yolk and water.

Manufacture.—Durum flour is moistened with water and mixed with a definite quantity of egg yolk. The dough is kneaded, rolled, cut into ribbons, dried as described for Minnesota Brand Amberolls—Elbow Macaroni (THE JOURNAL, Aug. 3, 1935, p. 369) and packed.

Analysis (submitted by manufacturer).—

	per cent
Moisture	9.0
Ash	1.2
Sodium chloride	0.3
Fat (acid hydrolysis method)	3.7
Protein (N × 6.25)	13.9
Water sol. protein-nitrogen precipitable by 40% alcohol	0.07
Lipoid phosphoric acid as P_2O_5	0.14
Crude fiber	0.5
Carbohydrates other than crude fiber (by difference)	71.7
Estimated commercial yolk solids	6.0

Calories.—3.8 per gram; 108 per ounce.

Claims of Manufacturer.—Conforms with U. S. Department of Agriculture definition and standard for egg noodles.

(1) BLUE RIBBON BRAND WHEAT CEREAL
(2) DEFIANCE BRAND WHEAT CEREAL
(3) NONE-SUCH BRAND WHEAT FOOD

Distributors.—(1) Oakford & Fahnestock, Peoria, Ill.; (2) Jobbers Service, Inc., Coldwater, Mich.; (3) Durand-McNeil-Horner Company, Chicago.

Packer.—Campbell Cereal Company, Northfield, Minn.

Description.—Wheat middlings, endosperm or farina.

Manufacture.—Wheat farina is obtained from flour mills, heated at 52 C. for thirty minutes to destroy any insect infestation and packed in cartons.

Analysis (submitted by packer).—

	per cent
Moisture	12.2
Ash	0.4
Fat (ether extraction method)	0.4
Protein (N × 5.7)	10.1
Reducing sugars as dextrose	0.5
Crude fiber	0.4
Carbohydrates other than crude fiber (by difference)	76.9

Calories.—3.5 per gram; 99 per ounce.

Claims of Distributors.—For use as a breakfast cereal or other table dishes; also for infant feeding as a carbohydrate supplement to milk under the directions of a physician.

DAISY BRAND CALIFORNIA PITTED PRUNES
DAPHNE BRAND CALIFORNIA PRUNES
HELIOTROPE BRAND CALIFORNIA PRUNES
LIBERTY BRAND PITTED PRUNES
MISSION BRAND CALIFORNIA PRUNES
PANSY BRAND CALIFORNIA PRUNES
PANSY BRAND LARGE SANTA CLARA PRUNES
PANSY BRAND MEDIUM SANTA CLARA PRUNES
PANSY BRAND SMALL SANTA CLARA PRUNES
PHOENIX BRAND CALIFORNIA PRUNES
ROSEDALE BRAND SANTA CLARA PRUNES

Packer.—Guggenhime & Company, San Francisco.

Description.—Partially dried, whole ripe prune plums, pitted or unpitted. See California Prunes Educational Advertising (THE JOURNAL, Nov 10, 1934, p. 1453).

PURINA WHOLE WHEAT FLOUR

Manufacturer.—Ralston Purina Company, St. Louis.

Description.—High protein whole wheat flour.

Manufacture.—High protein dark hard red winter wheat is cleaned of foreign material, milled to a definite granulation, retaining all the bran, embryo and endosperm, and packed in sacks.

Analysis (submitted by manufacturer).—

	per cent
Moisture	9.5
Ash	1.8
Fat (ether extraction method)	1.9
Protein (N × 5.7)	15.3
Crude fiber	2.2
Carbohydrates other than crude fiber (by difference)	69.3

Calories.—3.6 per gram; 102 per ounce.

Claims of Manufacturer.—Conforms to United States Department of Agriculture definition and standard.

1. GLENWOOD BRAND THOMPSON SEEDLESS RAISINS
2. GLENWOOD BRAND THOMPSON SEEDLESS RAISINS
MISSION BRAND THOMPSON SEEDLESS RAISINS

Packer.—Guggenhime & Company, San Francisco.

Description.—1. Sun-dried Thompson seedless grapes.

2. Thompson seedless grapes treated with a very small quantity of refined raisin seed oil.

Preparation.—1. The same as Gazelle Brand Seedless Raisins (THE JOURNAL, Jan. 26, 1935, p. 317).

2. The same as Gazelle Brand Seedless Raisins (THE JOURNAL, Jan. 26, 1935, p. 317) with the exception that these raisins are treated with a very small quantity of refined raisin seed oil to lessen adherence.

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SATURDAY, SEPTEMBER 21, 1935

DISEASE AND HISTORY

The reciprocal relations of disease and history not only provide food for philosophic speculation but offer much information worthy of study by the statesmen who direct the destiny of nations. The panorama produced by the effect of one on the other has been recently painted by Stewart.[1] He questions the historical justification of the relative amount of study devoted, for example, to Napoleon and to Pasteur or to Jenner. Which, he asks, more definitely made and molded history? One cannot question, he concludes, that disease and its gradual control are tremendously important molders of the history of mankind.

The first steps of the nomad in civilization, the gathering of houses into towns, doubtless trebled disease and cost innumerable lives. The principles of sanitation, though known to the ancient Hebrews, for centuries lagged far behind the advance in other lines of what we call civilization. Primitive communities were thus saved from extermination chiefly by their instinct for isolation. This fact has left primitive peoples relatively free from diseases and relatively immune to those which they did have. New diseases, however, brought to such groups have again and again practically annihilated whole populations. The introduction of a new relatively innocuous disease such as measles among the Boers resulted in the loss of one fifth of their numbers in concentration camps.

Travel, added to the concentration of peoples, ushered in a wider area for disease. The speed of travel closely paralleled the spread of disease and the march of civilization. In the second century A. D. it took plague forty years to reach China from the Red Sea. In the fall of 1888 an influenza epidemic was at Hongkong; by the beginning of the next November it was in St. Petersburg. But for modern preventive medicine, disease would now travel as fast as the airplane.

The effect of pestilences on individual communities and countries is a phase of historical study still largely undisturbed. Bubonic plague alone in the ten years that preceded 1907 carried off 6 millions in India, in 1910 was fatal to 46,000 in Manchuria and as late as 1923 killed a quarter of a million people, mostly in India. This was in modern times; but this destruction appears small in comparison with the havoc wrought by the Black Death. Villages and towns were left without inhabitants; in London 50,000 bodies were thrown into one burying ground; in a year in Europe 25 millions of people, half the population, died.

Such a convulsion must of necessity make history. That this resultant history is contradictory does not invalidate the thesis. The effect in England has been variously described. "Amid the general lamentation and woe the influence and authority of every law, human and divine, vanished." It paralyzed trade and industry, especially agriculture, but also paralyzed war and politics. "It detached people from the soil, drove them into the towns, increased urban population at the expense of rural, planted the germs of commerce and industry and began the expansion of England manifested in the time of Elizabeth." So with desolation came elbow room and opportunity.

The association between war and disease is as old as war itself. Sieges and campaigns have more often been decided by the race between pestilences in rival camps than by the force of arms. An invading army has brought pestilences that destroyed the invaders themselves first and sometimes the enemy. At other times the invaders acquired new diseases from the neutral or enemy countries through which they passed. "All that we gained in the end by engaging in the crusades," said Voltaire, "was the leprosy." As late as the Civil War, two Northern soldiers died of disease for every one who died by the weapons of the enemy. Such examples may be multiplied through all history.

These are examples of how disease has wrought history. The connection has always been close, not only in the lives of nations but also in the lives of individuals who make the history of nations. The gastric ulcer of a premier, the migraine of a foreign minister, the failing memory of a cabinet officer or the paranoia of a dictator may change in a brief period the economics, the history or the health of a nation.

1. Stewart, D. A.: Disease and History, Ann. M. Hist. **7**: 351 (July) 1935.

THE GENESIS AND CONTROL OF EPIDEMICS

So long as human beings are gregarious and prefer to live in crowded communities, they must contend with epidemics. In some modern centers of civilization there has developed a false sense of security in this regard. An epidemic is a disease of the crowd and may flare up like a forest fire. Modern preventive medicine and interest in public health measures have accomplished miracles in controlling herd infections. Nevertheless, calamity always is possible. Witness the recent terrific epidemic of malaria in Ceylon, where an enormous mortality rate has been recorded in a disease the cause of which is known and for which specific treatment is

available. The Chicago outbreak of amebiasis was significant. Consider the St. Louis epidemic of encephalitis and the recent outbreaks of poliomyelitis. Historically our concepts of epidemics may be grouped in two broad periods: (1) the descriptive period, when the natural history of epidemics was studied and correlated as to place, time and meteorological conditions; (2) the modern period, when the rise, subsidence and periodicity of epidemics is studied mathematically, graphically and even experimentally.

As Garrison [1] has indicated, the main protagonists of the former point of view were Hippocrates, Baillou and Sydenham. The modern theories have been expressed by Farr, Pearson, Ross, Greenwood and others. Sir Ronald Ross has classed epidemic diseases into (1) those of sluggish course and progression, such as leprosy or tuberculosis; (2) diseases of periodic recurrence, such as measles or scarlatina; (3) pandemic diseases, such as plague, cholera and influenza, which appear in full force at wide intervals of time. Gill,[2] a modern epidemiologist, has attempted a rational explanation of the genesis of epidemics. He finds that all epidemics and pandemics, irrespective of their parasitic cause or mode of spread, exhibit characteristic features as concerns geographic distribution, periodicity, seasonal incidence, wave form, diffusibility, toxicity, and special incidence in certain age groups. Gill maintains that there has been no demonstration of an exaltation of virulence of specific parasites in association with the rise of an epidemic. He presents the "quantum theory" as an explanation of the genesis of epidemics. This theory postulates that all epidemic manifestations are the outcome of loss of equilibrium between the dose of toxin and the degree of resistance, or between "infection" and "immunity." The effect of the introduction of living pathogenic organisms into the human body may be determined not only by the quantity of infection (dose) but also by the size (mass) and resistance (relative immunity) of the host. Circumstances conducive to a sudden increase of the infection quantum play a predominant part in determining epidemic outbursts. The quantum theory of Gill states that four factors are concerned in the origin of all epidemics: the reservoir, the parasite, the immunity, and the transmission factor. The actual occurrence of an epidemic is due to quantitative changes in equilibrium between "infection" and "immunity." This theory assumes the presence in all parasitic diseases of a reservoir of infection in which the specific parasite will be able to survive in a state of symbiosis with its host during periods adverse to its transmission. No instance is known of an epidemic disease in which either man or one of the lower animals does not constitute the reservoir. A given disease may be endemic in a community and at times epidemic. The disease may be considered hyperendemic, when infection and immunity are constant and high, or mildly endemic, when infection and immunity are constant and low. As concerns epidemicity there is first a preepidemic status, during which infection is long interrupted and immunity is absent. Then follows the epidemic status, when infection is constantly high and immunity is low. As mortality and morbidity subside, the postepidemic status is reached, when infection and immunity are both high. This is followed by the interepidemic status, characterized by intermittent infection in association with high herd immunity.

It is the duty of the epidemiologist to keep accurate records of the important herd diseases, chart their incidence and even attempt to predict their epidemic and pandemic occurrence under certain climatic, meteorological, social and economic conditions. However, the modern epidemiologist is not content with general biostatistical studies. He has begun to develop experimental epidemiology, a comparatively new science of extraordinary importance to the general health of communities and nations. Topley [3] in 1919 was probably the first modern epidemiologist to study disease as a mass phenomenon under experimental conditions. These pioneer studies were followed by similar though independent investigations by Flexner,[4] Amoss [5] and Webster.[6] Topley noted that breeds and individuals possess definite and different amounts of nonspecific inherited resistance to infection. This resistance is affected by environmental factors, such as season, diet and social and economic conditions, and may be supplemented by a specific acquired immunity. The amount of resistance present in individuals or populations at a given time determines the extent and severity of disease. Topley found that he could induce experimental epidemics in mice under two sets of conditions: (1) by administering to each individual of a previously unexposed community a certain dose of the specific organism by a natural port of entry or (2) by adding susceptible immigrants to already infected populations. He demonstrated that the repeated addition of normal individuals to mouse populations infected with Pasteurella is followed by recurring epidemic waves. Such experiments also afford an opportunity of analyzing the microbic and host factors under natural yet controlled conditions and of determining whether virulence actually varies during epidemics and whether epidemics terminate by the development of a specific immunity in the population. In these studies, bacterial strains from fatal cases manifested the same degree of virulence as similar strains from healthy carriers. This tends to prove Gill's contention that there is no noteworthy

1. Garrison, F. H.: The Newer Epidemiology, Mil. Surgeon **53**: 1 (July) 1923.
2. Gill, C. A.: The Genesis of Epidemics and the Natural History of Disease, New York, William Wood & Co., 1928.
3. Topley, W. W. C.: Goulstonian Lectures on the Spread of Bacterial Infection, Lancet **2**: 1 (July 5) 1919; The Milroy Lectures on Experimental Epidemiology, ibid. **1**: 477 (March 6) 1926.
4. Flexner, Simon: Experimental Epidemiology, J. Exper. Med. **36**: 9 (July) 1922.
5. Amoss, H. L.: An Artificial Induced Epidemic of Mouse Typhoid, J. Exper. Med. **30**: 25 (July) 1922.
6. Webster, L. T.: The Mode of Spread of a Friedländer Bacillus-like Respiratory Infection of Mice, J. Exper. Med. **47**: 685 (May) 1928.

exaltation of virulence under epidemic conditions. Further studies indicated that strains of bacteria recovered from a given population at various endemic and epidemic periods of spontaneous infection were of uniform virulence. Experimental epidemiology has apparently demonstrated that the virulence of a given bacterial strain, when analyzed under natural and under controlled conditions, is a relatively stable property. However, changes in dosage exerted a direct effect on mortality when virulence and resistance were constant. These results further tend to substantiate Gill's quantum theory as to the genesis of epidemics. Topley has demonstrated that an epidemic spreading slowly among an isolated herd will lead to a smaller total mortality than will another epidemic of the same disease that spreads rapidly within a short time of its onset. A herd among which an epidemic is spreading will approach extinction more rapidly if it is subjected to the immigration of susceptibles of the same species than if it is kept in isolation. In his experiments Topley found that a bacterial infection which tends to spread naturally may be maintained in an experimental herd for an indefinite period, provided the herd is replenished by immigration of susceptible animals even though the rate of immigration is very slow.

The movement of susceptible but uninfected individuals is one of the main factors determining the course and duration of the epidemic spread of bacterial disease. With the tremendous improvement in modern means of transportation, travel has increased to such an extent as to become a problem to guardians of the public health. As Stallybrass [7] has indicated, the principal bodies of migrating persons may be classed as (1) emigrants, (2) pilgrims, (3) transient laborers, (4) seafaring populations, railway and air personnel, (5) commercial travelers, merchants, itinerant traders, (6) tourists, (7) vagrants, (8) persons attending markets, fairs, musical or gymnastic contests, football or baseball matches and bull-fights, and (9) soldiers. The Chicago outbreak of amebic dysentery during the Century of Progress exposition is a comparatively recent example of the epidemic possibilities in travel and large gatherings. Leprosy has been found among Mexican railroad workers in Texas. Chinese workers, particularly those smuggled into the country, may act as a grave source of infection with leprosy, cholera, smallpox and amebic dysentery.

A study of the history of epidemics suggests that failure in prevention and control has been due to ignorance of causes and to lack of cooperation. The first essential in prophylaxis is an accurate knowledge of etiology. Then an adequate power of administration is required for education of the public and for effective control of causative factors. Preventive medicine is influenced at every point by the general social questions of education, economics and social welfare. Given a proper public health organization, the first necessity in control of an epidemic is early notification of cases as they occur. This implies complete cooperation on the part of all practicing physicians. Then the proper quarantine measures, isolation of contacts and carriers, and destruction or nullification of the reservoir of infection are carried out by the proper authorities. The most serious situations in such work are caused by the congested urban populations, the nodal centers of infection, and the slums, where overcrowding, insanitary conditions and ignorance result in endemicity of the infective disease. The incidence of infectious diseases and mortality from them are considerably greater in urban than in rural populations within the same geographic region. Increasing urban congestion and gregariousness is conducive to the development of epidemics. The best preventive measure is the destruction of slums and encouragement of the movement away from cities. The latter should be used merely for the purposes of commerce, while actual home life should be carried out under suburban and rural conditions.

Modern means of communication enable health authorities to keep informed of serious disease manifestations anywhere on the globe. International organization and cooperation are particularly necessary in this connection. In 1907 the Office international d'hygiène publique was established at Paris. By 1929 forty-nine countries had signed the agreement. The statistical bureau of the League of Nations was established at Geneva in 1919. Its weekly, monthly and annual bulletins contain information as to the incidence of plague, cholera, yellow fever, typhus, smallpox and other epidemic diseases. Because of congestion of population, poverty and climate, the Far East has always been a source of epidemics and pandemics. F. Norman White,[8] in his report to the Health Committee of the League of Nations on the prevalence of epidemic disease in the Far East, has studied the port procedures of maritime sanitation in various countries and has established a standard for class A ports from the standpoint of hygiene and prevention of epidemic disease. This standard requires that there be a qualified and adequate health staff, apparatus for fumigation of large vessels at anchor, a trained staff and means for the capture and extermination of rats, a quarantine station suitable for detention and observation of deck passengers and disinfection of their effects, an adequately equipped bacteriologic laboratory, an infectious disease hospital, a satisfactory water supply, and the machinery and legislation necessary for dealing with vital statistics, including the registration of cases and deaths from dangerous communicable diseases. White has suggested the creation of a central international epidemiologic intelligence bureau for the Far East to gather, correlate and render available the necessary data concerning contagious diseases and coordinate administrative measures in their

7. Stallybrass, C. O.: The Principles of Epidemiology and the Process of Infection, New York, Macmillan Company, 1931.

8. White, F. N.: The Prevalence of Epidemic Disease and Port Health Organization and Procedure in the Far East, Geneva, 1923.

control. There is no reason why such an organization cannot be truly international in scope and activity.

Modern epidemiology is a complex science devoted to a study of herd diseases, the conditions of their origin and the means for their control. It utilizes biostatistics and laboratory and field studies as well as administrative and legal powers in its efforts to understand and control epidemics. The physician at large may profitably broaden his hygienic vision by becoming epidemic minded. Such a physician will gladly report all transmissible diseases, out of duty to the community. His interest in the individual patient will be based on a broad understanding and sympathy with the aims of modern preventive medicine.

Current Comment

CAN THE LEOPARD CHANGE ITS SPOTS?

The "patent medicine" interests have decided that another housecleaning is called for. History repeats itself! Nearly thirty years ago, when the present national Food and Drugs Act was under consideration in Congress, the "patent medicine" people, through their publicity department, let it be known that all members of the "Proprietary Association of America"—as the organized "patent medicine" business was then called—would conform to certain rules of truthfulness and decency in advertising their wares. Unfortunately, the list of members of the Proprietary Association of America was never made public! About a year ago—in August 1934—there was published in the *Editor and Publisher* an article entitled "Proprietary Association Begins Clean-Up." In this it was stated that the Proprietary Association—the present name for the organized "patent medicine" interests—had created an Advisory Committee on Advertising, which would draw up an "Outline of Ethical Practices in Proprietary Advertising." In June of this year the New York *Times* reported that the Proprietary Association was about to "launch a comprehensive program of research." The function of this "Research Committee," it appears, is to gather evidence to rebut any damaging attacks on "patent medicines." The same article in the *Times* stated that Dr. Frederick J. Cullen, general representative of the Proprietary Association, was also serving, ex officio, as secretary. Dr. Cullen, as the *Times* pointed out, was formerly Chief of Drug Control of the Department of Agriculture. There has recently been issued (Aug. 28, 1935) what is presumably one of the first pieces of work in this field. In April 1933 the Department of Agriculture issued under Dr. Cullen's name a bulletin warning the public against the coated laxatives that contain phenolphthalein. The bulletin was a straightforward, valuable statement of fact, pointing out the potential dangers of phenolphthalein when used indiscriminately by the public in the form of "patent medicines" put up as "pressed fruits, mints, small cubes or lozenges" and "packaged attractively." Now (Aug. 28, 1935) the Proprietary Association, under Dr. Cullen's name, sends Bulletin 6365 to all its members. In this bulletin Dr. Cullen completely reverses himself on phenolphthalein. In it he states that the government bulletin (April 1933) issued by him was based on information gathered from medical textbooks and from a report made by a physician in one of the medical journals (the report of the case of a small child who ate a complete box of the "candy laxative" known as "Ex-Lax" and promptly died). It appears that Dr. Cullen today, in his connection with the "patent medicine" interests, has decided, "a more exhaustive study of the effects of phenolphthalein since the issuance of that article (April 1933) has resulted in a change in my opinion as to its harmful effects." This "exhaustive study" seems to have exhausted the doctor's judgment; one wonders where he found the new evidence on which the reversal of his opinion was based. Have new controlled studies been reported to warrant such a remarkable change of front or is there just a new job? Undoubtedly the "patent medicine" interests are on the defensive and presumably will spare no expense to convince a gullible public that its business is a public-spirited activity. But those who have followed critically the devious methods of the "patent medicine" business for more than a quarter of a century may be excused for holding to the well established opinion that the leopard does not change its spots.

THE PATHOMETRISTS

This month the Universal Society of Pathometrists held their sixth annual session. According to the newspapers that reported this notable event, "members are physicians who employ the pathoclast instrument, a vibratory mechanism used in diagnosis and treatment." Anybody who happened to read this item might have been convinced that the pathometrists were a new type of scientist representing a distinct advance over what scientific medicine has been able to accomplish in the diagnosis and treatment of disease. Nevertheless the pathometrists are merely a hybrid variety of the genus chiropractor. They are the chiropractors who use a device developed by the Pathometric Laboratories. The Pathometric Laboratories manufacture the pathoclast and the pathoneurometer. It appears that Dr. J. W. Wigelsworth of Los Angeles is the inventor of the pathoclast and also the founder of the Anabolic Food Products. Wigelsworth, whose name must have been an inspiration of a higher power, expands that cognomen by the letters "D.N.," which may mean "Doctor of Naprapathy" or "Doctor of Naturopathy." What a marvelous name for a vibrator promotion Wigelsworth really is! As far back as 1918 Wigelsworth was promoting a system of color and homeopathic diagnosis. With the passing of Abrams, the real originator of the "clast" and "meter" apparatus, Wigelsworth changed to his new machinery. The pathoclast appears as another of the fifty-seven varieties of imitations of the Abrams apparatus. The pathoneurometer was no doubt developed to compete with Chiropractor B. J. Palmer's neurocalometer. Using a phrase popularized by that master of comedy Ben Bernie, the "anabolic foods" are the nuts!

Association News

RADIO BROADCASTS

The American Medical Association will broadcast over the Blue network of the National Broadcasting Company at 5 p. m. eastern standard time (4 o'clock central standard time, 3 o'clock mountain time) October 1 and each Tuesday thereafter, presenting a dramatized program with incidental music under the general theme of "Medical Emergencies and How They Are Met." The title of the program will be Your Health. The program will be recognizable by a musical salutation through which the voice of the announcer will offer a toast: "Ladies and Gentlemen, Your Health!" The theme of the program will be repeated each week in the opening announcement, which informs the listener that the same medical knowledge and the same doctors that are mobilized for the meeting of grave medical emergencies are available in every community, day and night, for the promotion of the health of the people. Each program will include a brief talk dealing with the central theme of the individual broadcast.

The October schedule is as follows:

October 1. Burns, Morris Fishbein, M.D.
October 8. Hazards from Foreign Shores, W. W. Bauer, M.D.
October 15. Unconsciousness, Morris Fishbein, M.D.
October 22. Asphyxiation, W. W. Bauer, M.D.
October 29. Poisonous Plants and Insects, W. W. Bauer, M.D.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION, PUBLIC HEALTH, ETC.)

COLORADO

Promotions at Medical School.—Dr. James M. Shields, associate professor of ophthalmology, and Dr. Claude E. Cooper, associate professor of otolaryngology, have been appointed heads of their departments at the University of Colorado School of Medicine, Denver.

Memorial for Physician.—The Pueblo Clinical and Pathological Society recently presented a check for $30 to the library of the Medical Society of the City and County of Denver to purchase new medical books in memory of Dr. Seymour D. Van Meter, a past president of the latter society. Each book purchased with this money will be inscribed: "This book is presented to the library in memory of S. D. Van Meter, M.D., by the Pueblo Clinical and Pathological Society." Dr. Van Meter died in February 1934. For many years he was secretary of the state board of medical examiners.

State Medical Election.—Dr. Walter W. King, Denver, was installed as president of the Colorado State Medical Society at the annual meeting in Estes Park, September 4-7. Dr. Arthur J. Markley, Denver, was chosen president-elect and vice presidents elected are Drs. Leo W. Bortree, Colorado Springs; Herman C. Graves, Grand Junction; Archie C. Sudan, Kremmling, and Clarence W. Bixler, Erie. The next annual session will be held in Glenwood Springs, Sept. 9-12, 1936, with headquarters in the Hotel Colorado. There were 375 members of the society, guests and nonmembers and 176 other persons registered at the meeting.

GEORGIA

Dr. Crile to Give McRae Lecture.—Dr. George W. Crile, Cleveland, will present the Floyd Wilcox McRae Memorial Lecture of the Fulton County Medical Society, October 11. His address will be entitled "The Genesis and Practice of Medicine."

Births and Deaths Increase.—A total of 65,615 live births were registered in Georgia in 1934, as compared with 60,744 in 1933, according to the state department of health. An increase of 4,406 deaths was recorded for 1934, a total of 35,590 deaths for the year as compared with a total of 31,184 in 1933. The infant mortality rate showed an increase of 17.1 per cent, it was stated; the rate in 1934 was 78.7 per thousand live births, in comparison with 67.2 in 1933.

ILLINOIS

Society News.—At a meeting of the Peoria City Medical Society, September 3, speakers included Drs. William A. Malcolm on endometriosis; Hugh E. Cooper, backache; Walter H. Baer, early symptoms and treatment of dementia paralytica, and John M. McCuskey, common skin diseases. Dr. Nelson M. Percy, Chicago, addressed the society, September 17, on "Surgery of the Superior Hypogastric Plexus of the Sympathetic Nervous System."——At a meeting of the Jefferson-Hamilton County Medical Society, Mount Vernon, a symposium on obstetrics was presented by Drs. Thomas B. Williamson, Harry G. Thompson, William G. Parker, all of Mount Vernon; Frank B. Hiller, Pinckneyville, and John Beverly Moore, Benton.——Dr. Max S. Wien, Chicago, addressed the Stephenson County Medical Society at Freeport, August 28, on "Relation of Dermatology to General Medicine."

Chicago

Dr. Coutard to Give McArthur Lecture.—Dr. Henri Coutard, chief of the department of roentgen therapy of cancer, Curie Institute, University of Paris, will deliver the twelfth Lewis Linn McArthur Lecture of the Frank Billings Foundation of the Institute of Medicine of Chicago, October 1, at the Chicago Woman's Club. The subject of his illustrated lecture will be "The Conception of Periodicity as a Possible Directing Factor in the Roentgen Therapy of Cancer." The meeting will be a joint session with the Chicago Laryngological and Otological Society.

INDIANA

Physicians in Chamber of Commerce.—Members of the Montgomery County Medical Society, at a meeting July 25, voted to form an organized division of the Crawfordsville Chamber of Commerce. According to the *Journal of the Indiana State Medical Association*, this group will serve as a separate organization from the county medical society and its activities will be centered on business problems of the profession.

IOWA

Personal.—Dr. Philip I. Crew has been appointed health officer of Marion.——Dr. Willard W. Hayne, Des Moines, has been appointed medical supervisor of athletics at the State University of Iowa, Iowa City, succeeding Dr. Arthur S. Fourt.

Society News.—The Louisa County Medical Society held a fish fry at Chautauqua Park, Columbus, August 8.——Dr. Harold B. Cushing, Montreal, Canada, will discuss "Prevention and Treatment of Scarlet Fever" before the Linn County Medical Society, Cedar Rapids, October 16.——Dr. John F. Erdmann, New York, addressed the Des Moines Academy of Medicine and the Polk County Medical Society, September 13, on "Common Duct Injuries and Their Reconstruction."

KANSAS

Advisory Committee for Health Projects.—Drs. Barrett A. Nelson, Manhattan, and Forrest L. Loveland, Topeka, have been appointed representatives of the state medical society on an advisory committee to study health projects to be undertaken with funds made available under the Social Security Act. The committee is composed of representatives from the medical, dental, hospital and nursing professions of the state.

Dr. Brown Made Professor of Hygiene.—Dr. Earle G. Brown, Topeka, since 1925 secretary of the Kansas State Board of Health, has been appointed professor of hygiene and preventive medicine at the University of Kansas School of Medicine, Kansas City. Dr. Brown graduated from Northwestern University School of Medicine, Chicago, in 1913, and engaged in private practice in Topeka from 1914 to 1917. In 1919 he was appointed health officer of Topeka, serving in this capacity until he was appointed secretary of the state board of health. Dr. Brown will retain his position with the state board.

Deaths of Physicians.—In a study of the deaths of 170 Kansas physicians reported in the last four years, chronic myocarditis was found to be the leading cause of death, being responsible for twenty-seven deaths, according to the state medical journal. Cancer and chronic nephritis were second; diabetes and coronary thrombosis were fourth; cerebral hemorrhage was sixth. Motor vehicles caused five of the seven accidental deaths. Excluding deaths from violence, the average age at death was 67.3 years. The oldest was 96. Excluding deaths from external violence, sixty-one deaths, or 41 per cent, were attributed to diseases of the cardiovascular system. Of the 20,011 deaths of all persons reported in the state in 1934, only 25 per cent were due to cardiovascular disease.

KENTUCKY

State Medical Meeting at Louisville.—The eightieth annual session of the Kentucky State Medical Association will be held in Louisville at the Brown Hotel, September 30 to October 3. The annual oration will be delivered by Dr. Sumner L. S. Koch, Chicago, at the banquet Wednesday evening, October 2, on "Injuries to the Hand." The oration in surgery will be given by Dr. Samuel C. Smith, Ashland, and the oration in medicine by Dr. James H. Pritchett, Louisville. Among papers to be presented are the following:

Dr. Ernest B. Bradley, Lexington, Evaluation of the Newer Methods of Handling Pulmonary Tuberculosis.
Dr. Rockwell Emerson Smith, Henderson, Contract Practice.
Dr. Joseph D. Northcutt, Covington, Social Trends in Medicine.
Dr. James Duffy Hancock, Louisville, Modern Management of Tumors of the Breast.
E. D. Rose, D.D.S., University of Tennessee College of Dentistry, Memphis, What the Physician Should Know About Periodontal Lesions.
Dr. Wilford A. Risteen, Lebanon, Diet in Relation to Abdominal Infections.
Dr. Harry D. Abell, Paducah, Ocular Manifestations of Systemic Disease.
Dr. Benjamin F. Wright, Seco, Emergency Management of Fractures.

There will also be a symposium on obstetrics presented by Drs. Scott D. Breckenridge, Lexington, Charles L. Sherman, Millwood, and Amplias W. Davis, Madisonville. Dr. Joshua B. Lukins, Louisville, will deliver his presidential address at a public meeting Tuesday evening, October 1, at which also Judge Elwood Hamilton, Louisville, will speak.

MICHIGAN

Graduate Courses.—The University of Michigan Medical School, Ann Arbor, and the Michigan State Medical Society will open a series of short graduate courses, September 30, in Grand Rapids, Flint, Bay City, one jointly for Battle Creek and Kalamazoo, and one for Manistee, Traverse City and Cadillac. By request of Upper Peninsula physicians, the program for that section will be deferred until May 1936. The courses will be held one day a week for eight weeks, the week of October 14 to be omitted to permit attendance at the Inter-State Postgraduate Medical Assembly in Detroit. Subjects will include maternal welfare, gynecology, pulmonary disease, diseases of joints, neuropsychiatry, metabolic diseases, diseases of the blood and blood-forming organs, child welfare, skin diseases, cancer, genito-urinary diseases, anorectal diseases, fractures and biliary tract disease. One week courses will be conducted at Detroit and Ann Arbor. Information may be obtained from the department of graduate medicine, University Hospital, Ann Arbor.

MINNESOTA

Society News.—Dr. Arthur N. Collins, Duluth, was elected president of the Northern Minnesota Medical Association at its annual meeting, August 12, succeeding Dr. George I. Badeaux, Brainerd. The next annual meeting will be held in Fergus Falls.

Health Survey.—Of the $3,450,000 federal allocation for a national public health survey, Minnesota will receive $108,500 to carry out its studies, newspapers report. A house to house canvass will be made to determine the prevalence of chronic diseases; physical examinations will be given and studies of medical facilities will be carried out.

Dr. Wangensteen Awarded Philadelphia Prize.—The Samuel D. Gross Prize for 1935 has been awarded to Dr. Owen H. Wangensteen, professor of surgery, University of Minnesota School of Medicine, Minneapolis, for an essay entitled "The Therapeutic Problem in Bowel Obstruction." The prize is awarded every five years by the Philadelphia Academy of Surgery to the writer of the best original essay on surgical pathology or surgical practice founded on original investigations.

NEW JERSEY

Hospital News.—The new Zurbrugg Hospital, Riverside, with a capacity of forty beds, was opened recently after a delay of three years. The hospital was built with funds left by Theophilus J. Zurbrugg, but no money was available for operating expenses until the Burlington County Board of freeholders agreed to aid in its maintenance. The institution has been in operation since 1915 with a capacity of twelve beds.

Society News.—Dr. Arthur C. Christie and Ross Garrett, Washington, D. C., addressed the Essex County Medical Society, Newark, September 12, on "Coordination of Resources for Medical Care."——Dr. Albert F. R. Andresen, Brooklyn, and Lloyd K. Riggs, Ph.D., Rutgers University, New Brunswick, addressed the Bergen County Medical Society, Hackensack, September 10, on "Focal Infection" and "Evaluation of Antiseptics in Modern Practice," respectively.

NEW MEXICO

District Health Organization.—Health work in New Mexico has been organized into ten districts, each under the supervision of a full time health officer. Nine officers have already been appointed, with headquarters as follows: Drs. Elroy F. McIntyre, Santa Fe; Edgar B. Beaver, Gallup; James R. Scott, Albuquerque; Charles W. Gerber, Las Cruces; William W. Johnston, Las Vegas; Owen E. Puckett, Carlsbad; Frank W. Parker Jr., Silver City; Julian O. Long, Los Lunas, and Leonard A. Dewey, Clovis (temporary).

NEW YORK

Society News.—Dr. Spencer T. Snedecor, Hackensack, N. J., addressed the Suffolk County Medical Society, Sayville, July 31, on treatment of burns.——The program of the Westchester County Medical Society, September 17, was presented by members of the staff of Grasslands Hospital, Valhalla, Drs. William G. Childress, White Plains, Morley T. Smith and George C. Adie, New Rochelle, who gave a symposium on bronchiectasis.

New York City

Hospital News.—Dr. Béla Halpert, assistant professor of pathology and surgery, Yale University School of Medicine, New Haven, Conn., has been appointed head of the division of pathology and associate director of laboratories at the Jewish Hospital of Brooklyn.——Misericordia Hospital opened a new radiology department July 24. It has units for high voltage therapy, diagnostic radiography, fluoroscopy, urology and fracture work.

Personal.—Dr. Alix Churchill, associate secretary-general of the International Association for Prevention of Blindness and executive secretary of the International Union Against Tuberculosis, recently arrived in the United States for a series of conferences in various cities on policies and procedures in the world-wide fight against blindness and tuberculosis. Dr. Churchill is the guest of the National Society for the Prevention of Blindness and the National Tuberculosis Association.

City Collects for Accident Cases.—Special efforts by the department of hospitals to obtain reimbursement for the city in accident cases in which victims have been cared for in municipal hospitals have resulted in steadily increased collections during the current year, the department reports. In December 1934 the collections amounted to $930 and by June they had increased to $5,688. A total of 4,500 potential liability cases have been referred to the department since October 1934. Of this number 650 were closed after investigation because of nonliability or an insolvent defendant; about 1,500 cases in which the department has an interest are now pending. The department also reported that collections had been made in 179 cases not in court.

Positions Open in Health Department.—Open competitive examinations for two positions in the New York City Department of Health, research pediatrician (tuberculosis immunization) and epidemiologist, are announced by the Municipal Civil Service Commission. The pediatrician is expected to continue investigations already under way on the use of the Calmette or B C G vaccine, conduct research on pneumonia serums and similar problems. Requirements include graduation from a recognized medical school, experience in the use of vaccines and serums, including specialized experience with B C G vaccine. The salary is $3,000 a year. Duties of the epidemiologist will be to investigate incipient outbreaks of communicable illness and terminate the transmission of infection at the earliest possible moment. Requirements include graduation from a recognized medical school and two years of special training or experience in epidemiologic work in a state or city health department or the equivalent. The salary is $5,500 a year. For both positions candidates must have licenses to practice medicine in New York before they can be certified. Candidates must be between 25 and 50 years old. Applications will be received until October 2. Further information may be obtained from William H. Allen, secretary of the civil service commission, Room 1400, Municipal Building, Manhattan.

NORTH CAROLINA

Society News.—Dr. Verling K. Hart, Charlotte, addressed the Guilford County Medical Society, Greensboro, August 1, on "Bronchoscopic Observations on Bronchial Obstruction and Bronchiectasis."——Speakers at the regular meeting of the Catawba Valley Medical Society, Morganton, September 10, were Drs. Lester A. Crowell Jr., Lincolnton, on "Vaccination for Poliomyelitis"; Samuel F. Ravenel, Greensboro, "Nervous Children," and D. Lesesne Smith, Spartanburg, S. C., "Acute Infectious Diseases and Diarrhea in Children."

Report of Duke Hospital.—The annual report of Duke Hospital, Durham, states that 80 per cent of its patients in 1934 came from counties outside of Durham; ninety-three of the 100 counties in the state were represented. During 1934 the hospital cared for 236 patients a day at a cost of $385,782. The patients paid 43.5 per cent of the cost, counties and cities contributed 3.4 per cent, other contributions amounted to 3.1 per cent, and the hospital made up the remainder from its endowment. The outpatient department reported 40,949 visits.

OHIO

Personal.—Dr. Joyce I. Hartman has been appointed supervisor of health education in the Cleveland public schools, succeeding Dr. Lyman W. Childs, who had held the position since 1910.

Hospital News.—Babies' and Children's Hospital, Cleveland, one of the University Hospitals group, was to be reopened August 5, after having been closed for two years as an economy measure. Dr. Henry J. Gerstenberger will head the department of pediatrics and Dr. Carl H. Lenhart, the department of surgery.

Society News.—Drs. Ralph H. Major, Kansas City, Mo., and Max M. Peet, Ann Arbor, Mich., addressed the Cleveland Academy of Medicine, September 20, on medical and surgical aspects, respectively, of arterial hypertension.——Dr. Philip H. Kreuscher, Chicago, addressed the Summit County Medical Society, Akron, September 3, on "Back Injuries and Inflammations."——Dr. Walter M. Simpson, Dayton, discussed fever therapy before the Greene County Medical Society, Xenia, August 1.

Rock Gardens and the Malaria Increase.—Eighty-five cases of malaria have been reported to the state health department in the first eight months of the year, thirty-four of them in July and thirty-eight in the first twenty-three days of August. In 1934 there were 104 cases. *Ohio Health News* points to the current fad for rock gardens as one of the causes for an increase of the anopheles mosquito; the hollows and crevices in the rocks provide facilities for development. Other causes are a similar fad for small pools as water gardens and fish ponds, carelessness in leaving empty cans, bottles and discarded automobile tires about houses and, in the country and small villages, continued use of the old-fashioned rain barrel.

OREGON

Society News.—Dr. James Tate Mason, Seattle, President-elect, American Medical Association, addressed the Eastern Oregon Medical Society at a meeting in Ontario, July 27.

Personal.—Drs. F. Floyd South and Archie C. Van Cleve, Portland, have been appointed to the state board of health to succeed Drs. Albert Mount, Oregon City, and Joseph P. Brennan, Pendleton, respectively.

Health Officers' Conference.—A conference of city and county health officers was held in Portland, September 16-18. Mornings were given over to clinics at the University of Oregon Medical School, covering antepartum and postpartum conditions and venereal disease. The first afternoon program included discussions of blindness, heart disease, cancer and medical dentistry; the second, venereal disease, and the third, maternal and child health. Among speakers were Drs. Frederick A. Kiehle, Homer P. Rush, Thomas A. Davis, Morris L. Bridgeman, Lendon Howard Smith, all of Portland, and Edith P. Sappington of the U. S. Children's Bureau.

PENNSYLVANIA

District Meeting at Reading.—The second councilor district of the Medical Society of the State of Pennsylvania held its annual meeting at the Reading Country Club, September 19. The scientific program included papers by Drs. Philip F. Williams, Philadelphia, on "Intrapartum Care in Relation to Maternal Mortality"; Clarence A. Patten, Philadelphia, "Mental Hygiene Viewpoints on Sterilization of the Unfit"; Moses Behrend, Philadelphia, "Collapse Therapy in Pulmonary Tuberculosis," and Brig. Gen. Matthew A. DeLaney, commandant of Carlisle Barracks, "What the Medical Department of the U. S. Army Has Contributed to Human Progress." Speakers on organization problems were Drs. William H. Mayer, Pittsburgh, on public relations; Francis F. Borzell, Philadelphia, medical service plans; George L. Laverty, Harrisburg, emergency medical relief, and Chauncey L. Palmer, Pittsburgh, legislative problems concerning public health. Testimonials were presented to three members who have practiced medicine fifty years: Drs. Anthony F. Myers, Blooming Glen; Josiah B. Keylor, Cochranville, and Levi S. Walton, Jenkintown.

Philadelphia

Hospital News.—Dr. Frank E. Leivy delivered the first of a series of public health lectures at Mount Sinai Hospital, September 18, on "What You Should Eat and Why." Dr. Joseph Edeiken will give the second lecture, October 16, on "Heart Disease: Its Prevention and Care."

SOUTH CAROLINA

Graduate Assembly in Anderson.—The first Piedmont Post Graduate Clinical Assembly was held at the Anderson County Hospital, Anderson, September 3-5, with the following program:

Dr. William A. Mulherin, Augusta, Ga., Preventive Pediatrics.
Dr. Richard M. Pollitzer, Greenville, Infantile Paralysis.
Dr. D. Lesesne Smith, Spartanburg and Saluda, N. C., Everyday Pediatrics.
Dr. Joseph Warren White, Greenville, Recent Progress in the Care of Hip Fractures.
Dr. George H. Bunch, Columbia, Suppurative Pericarditis.
Dr. A. Johnson Buist, Charleston, Cancer of the Colon.
Dr. Joseph H. Cannon, Charleston, Practical Points in Diagnosis and Treatment of Heart Disease.
Dr. Kenneth M. Lynch, Charleston, Pathology of Common Cardiac Lesions.
Dr. Allen I. Josey, Columbia, Differential Diagnosis of Chronic Digestive Disorders.

One session was held jointly with the South Carolina division of the Southeastern Surgical Congress. At a banquet meeting with the Anderson County Medical Society, speakers were Drs. Samuel E. Harmon, Columbia, president of the South Carolina Medical Association, on "Relationship Between Public Health and Government Activities and the Practice of Medicine"; Kenneth M. Lynch, Charleston, "Doctors for South Carolina," and Foster M. Routh, Columbia, "The County Health Unit." The assembly was organized last April for graduate instruction of physicians with Dr. Edgar A. Hines, Seneca, president; Dr. Jack D. Parker, Greenville, vice president, and Dr. Archer L. Smethers, Anderson, secretary.

WASHINGTON

State Medical Election.—Dr. Delmar F. Bice, Yakima, was elected president of the Washington State Medical Association at the annual session at Everett in August. Dr. Curtis H. Thomson, Seattle, was reelected secretary. Next year's meeting will be held in Yakima.

WISCONSIN

Personal.—Citizens of Mauston held a public reception July 21 in honor of Dr. James S. Hess Sr., who has retired after forty-two years of medical practice. A silver plaque was presented to Dr. Hess, who is 70 years old.——Dr. Harry P. Bowen has been appointed postmaster of Watertown for a four year term.

Position Open for Health Officer.—The state bureau of personnel, Madison, announces an open competitive examination for the position of assistant state health officer, open to candidates who are citizens of the United States and who have been residents of Wisconsin for one year. Minimum qualifications are as follows: training equivalent to that represented by graduation from a medical school of recognized standing, with special training in the field of tuberculosis prevention and other public health work; possession of, or eligibility for, a valid license to practice medicine in Wisconsin; extended professional experience, five years of which shall have been in responsible public health and related work; familiarity with accepted methods and practices in preventive medicine; ability as a public speaker; administrative ability, tact, judgment and good physical condition. Applications will be received until September 28.

Community Honors Dr. Nuzum.—The Rock County Medical Society, the Janesville Civic and Industrial Council and the staff of Mercy Hospital sponsored a "Golden Medical Holiday," September 17, in honor of Dr. Thomas W. Nuzum, who has completed fifty years in the practice of medicine. At a public testimonial dinner in the evening at the Janesville High School, Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, made an address on "Medical Progress in the Last Fifty Years." In the morning there were surgical clinics, including an operation performed by Dr. Nuzum, and clinical conferences in the various departments of Mercy Hospital. After a luncheon at the Janesville Country Club, a scientific program was presented which included papers by Dr Franklin R. Nuzum, Santa Barbara, Calif., read by Dr. Thomas Ochsner Nuzum, Janesville, and Dr. John W. Nuzum, Chicago, all sons of the guest of honor. Other papers were read by Drs. Nelson M. Percy and Harry Culver, Chicago, and Dr. Joseph S. Evans, Madison.

Dr. Nuzum was born in Viroqua, Aug. 27, 1860; was graduated from Rush Medical College, Chicago, in 1885, and practiced in Albany and Brodhead before going to Janesville in 1906. During the World War he served as a first lieutenant at Fort Sheridan, Ill., and later at Camp Custer, Mich. Dr. Nuzum's three sons are all graduates of their father's alma mater.

ALASKA

Dr. DeVighne Leaves Alaska.—After more than thirty years' practice in Alaska, Dr. Harry C. DeVighne is moving to Santa Barbara, Calif. Dr. DeVighne was secretary of the Alaska Board of Medical Examiners for twenty years; twelve years commissioner of health, which position he resigned in 1934; fifteen years secretary of the Territorial Medical Association, and seven years chief surgeon of the Alaska Juneau Gold Mining Company. Dr. William P. Blanton, Juneau, will succeed Dr. DeVighne as secretary of the association and in the mine medical work.

PUERTO RICO

Fellowships to Puerto Ricans.—Eight Puerto Ricans were recently designated by Dr. Eduardo Garrido Morales, commissioner of health, to receive fellowships granted by the Rockefeller Foundation's International Health Division for study in the United States. Those chosen are Drs. Norberto A. Quinones, who will study bacteriology; Juan Basora and Victor J. Montilla, public health; Abel de Juan, vital statistics and epidemiology; Jose R. Vivas and Libertad R. Gaetan, tuberculosis, and Misses Winifred M. Mendez and Carmen L. Rivera, public health nursing.

GENERAL

Grants Available for Research.—The division of medical sciences of the National Research Council will hold a special meeting in November for the consideration of applications for grants in the field of medicine. Applications must be on file with the secretary of the Committee on Grants-in-Aid, Clarence J. West, Ph.D., 2101 Constitution Avenue, Washington, D. C., not later than October 1. Applications received after October 1 and before Feb. 1, 1936, will be acted on at the next regular meeting in March 1936.

Poliomyelitis Declines.—The New York City Department of Health reported September 15 that 238 cases of poliomyelitis had been reported during the week ended September 13, compared with 289 for the preceding week. The high point of the outbreak was reached during the week ended August 30, when 359 cases were reported. The total for the year was 1,552, with fifty-nine deaths, it was reported September 11. ——Fifty-five active cases were reported from Louisville, Ky., September 2; the total since June 15 is seventy-four. Two deaths have occurred.

Health Education Institute.—The American Public Health Association's fourth health education institute will be held in Milwaukee, October 4-6, preceding the annual session of the association. The subject of this year's institute will be "Health Education, with Special Reference to Smaller Cities and Rural Communities." Leaders of the discussions will be W. Frank Walker, Dr.P.H., director of the division of health studies, Commonwealth Fund, New York; Wesley Maurer of the school of journalism, University of Michigan, Ann Arbor; Evart G. Routzahn, editor of the public health education section of the *American Journal of Public Health*, and Ruth E. Grout, Cattaraugus County School Health Service, Olean, N. Y.

Resolution on Professional Relationships.—At its recent annual meeting in Portland, Ore., the American Pharmaceutical Association adopted a resolution expressing "the belief that it is essential to good medical care and to the welfare of the public that the personal relation between those engaged in the practice of medicine, dentistry, pharmacy and allied professions and their clientele be preserved." The action was taken, the resolution said, in view of the fact that certain proposed methods of providing medical care to the public through federal, state and private agencies contemplate corporate practice involving elimination or serious interference with the personal and private relations between members of the medical, dental, pharmacal and nursing professions and their clientele.

Society News.—Dr. Roscoe C. Giles, Chicago, was elected president of the National Medical Association at its annual session in New Orleans in August. Dr. John T. Givens, Norfolk, Va., William D. Giles, D.D.S., Chicago, and Emile J. La Branche, New Orleans, were elected vice presidents and Dr. Charles A. Lanon, South Brownsville, Pa., secretary. Next year's meeting will be held in Philadelphia.——The Western Orthopedic Association will hold its annual session at San Francisco, October 25-26, with a program of addresses and clinical meetings at San Francisco, Stanford and Mount Zion hospitals. Dr. Merrill C. Mensor, 490 Post Street, San Francisco, is secretary.——Dr. Henry E. Young, Victoria, B. C., was elected president of the Western Branch of the American Public Health Association at its recent annual meeting at Helena, Mont., and Dr. William P. Shepard, San Francisco, secretary. Next year's meeting will be held in Vancouver, B. C.——The Central Association of Obstetricians and Gynecologists will hold its seventh annual meeting in Omaha, October 10-12, at the Hotel Fontenelle.——The American Dermatological Association will hold its next annual meeting at the New Ocean House in Swampscott, Mass., June 4-6, 1936. ——The twenty-fourth annual Safety Congress and Exposition will be held in Louisville, Ky., October 14-18.——The International Medical Assembly of the Interstate Postgraduate Medical Association of North America will be held in Detroit, October 14-18, with headquarters at the Masonic Temple.—— The Society for Plastic and Reconstructive Surgery will hold its annual meeting at the Hotel Statler, Detroit, October 18-19.

American Hospital Association.—The annual session of the American Hospital Association will be held in St. Louis, September 30 to October 4, under the presidency of Robert Jolly, Houston, Texas. Among physicians listed on the program for addresses are:

Dr. H. Kennon Dunham, Cincinnati, Interpretation of Chest Films, with Special Reference to Tuberculosis.
Dr. Evarts A. Graham, St. Louis, Differential Diagnosis of Chest Films.
Dr. Williams McKim Marriott, St. Louis, Conduct of a Convalescent Department of a Children's Hospital.
Dr. Robinson Bosworth, Rockford, Ill., Rehabilitation of Patients in the Sanatorium.
Dr. Magnus C. Petersen, St. Peter, Minn., The Hospital Library in Relation to Psychiatric Research.
Dr. George Harvey Agnew, Toronto, Governmental Methods of Providing Care for the Indigent Sick in Canada Compared with the United States.
Dr. Nathaniel W. Faxon, Boston, Past, Present and Future Status of Governmental Hospitals in the Care of the Indigent Sick and Their Relation and Effect on Nongovernmental Public Hospitals.

The American Protestant Hospital Association will hold its meeting in St. Louis September 28-30, and the American Occupational Therapy Association will meet simultaneously with the American Hospital Association.

Death Rates in 1934.—The U. S. Bureau of the Census announces that there were 1,396,903 deaths in the United States in 1934, a mortality rate of 11 per thousand estimated population, an increase over the rate for 1933, which was 10.7. The bureau has issued a comparative summary of mortality statistics for the last three years, giving mortality rates for all causes of death. The tuberculosis death rate fell from 62.9 per hundred thousand of population in 1932 to 56.6 in 1934, while the rate for cancer and other malignant tumors rose from 102.2 to 106.3 in the two years. The type of cancer most frequently found was that of the digestive tract and peritoneum. Deaths from diabetes increased from 26,368 to 28,000, the rate from 22 to 22.1. The number of deaths from cerebral hemorrhage increased from 94,694 to 97,148. Diseases of the circulatory system caused 333,296 deaths in 1934, compared with 295,509, an increase in rate from 246 to 263.6 per hundred thousand; most numerous were diseases of the myocardium, which caused 136,726 deaths in 1934. The pneumonia death rate was 41.2 in 1932 and 43.3 in 1934 but was 36.4 in 1933. Appendicitis deaths rose slightly, 18,129 in 1934 as compared with 17,111 in 1932. A decrease was shown in deaths from pregnancy, childbirth and the puerperal state, the rates for the three years being 11.1 for 1932, 10.3 for 1933, and 10.2 for 1934. Suicides also showed a downward trend, the rates being 17.4, or 20,927 deaths, in 1932, 15.9, or 19,993 deaths, in 1933, and 14.9, or 18,828 deaths, in 1934. On the other hand, homicides rose from 11,035, or a rate of 9.2, in 1932 to 12,055, or 9.5, in 1934. Primary automobile accidents caused 33,980 deaths in 1934, compared with 29,323 in 1933 and 26,350 in 1932. Air transportation accidents caused 428 deaths in 1934, compared with 434 in 1933 and 386 in 1932. All violent and accidental deaths increased from 117,830 in 1932 and 123,204 in 1933 to 132,022 in 1934.

CORRECTION

Antimeningococcic Antitoxin.—In a news item concerning the recent retirement of Dr. Simon Flexner, published in THE JOURNAL, June 22, page 2274, the statement was made that Dr. Flexner "was the first to use the meningococcus antitoxin." The term "antimeningitis serum" should have been used, as the statement referred to Dr. Flexner's early work on that serum and not to the recent antitoxin developed by Ferry and used by Hoyne (THE JOURNAL, March 23, p. 980).

Foreign Letters

LONDON

(From Our Regular Correspondent)

Aug. 24, 1935.

Defense of the Civil Population Against Gas Attacks

Further information is now available concerning precautions against gas attacks on the civilian population. The St. John Ambulance Brigade is making comprehensive provision. A scheme of education and training will be in full operation by the autumn. It will include instruction of householders in precautionary measures and the formation of an air raids precautions reserve. Selected officers of the brigade from every county have already been given an intensive course of training, and virtually all the personnel of the London district—some 7,000 men and women—are now instructed in anti-gas precautions and first aid in cases of gas poisoning. The brigade is appointing an officer for every county throughout the country and also for every municipal borough. The duties of these anti-gas precautions officers, as they are called, will be important. After thorough training they will be available in their own areas to advise local authorities as to the safeguarding of the civil population. They will supervise the dissemination of knowledge among householders, who will then be in a position to afford their families all the protection possible against poison gas. They will also organize the air raids precautions reserve. It is believed that many citizens who have not time or inclination to join the brigade as members would be prepared in times of emergency to lend a hand in combating the effects of gas. They will be invited to enroll. Their training will be based on the instruction in the official handbook.

The further task of educating the civil population in anti-gas precautions has been begun by a demonstration showing how a householder can make one of his rooms secure against explosive blasts, metal splinters and poison gas for an expenditure not exceeding $5. Boarded windows and protective curtains over the doors are the only external evidence that the house is equipped to stand a gas attack. Inside, a back bedroom has been completely fitted as a shelter and contains everything needed for a prolonged occupation—canned foods, drinking water, beds, furniture, a wireless set for receiving news, books and games to pass the time, utensils containing the liquid with which the protective curtains over the door and windows must be kept damp, a garden syringe for spraying the curtains, and gas masks for use if the occupants go out of the room or for emergencies. The masks, of a type approved by the government, are said to remain gas tight for sixty hours. It is asserted that a room so protected and furnished may be occupied for several days.

Investigation of Industrial Dust Diseases

An important advance in the investigation of industrial dust diseases such as silicosis has been made by the invention of a thermal precipitator by Prof. R. W. Whytlaw-Gray and Dr. R. F. Lomax. During investigations of exposure of stone masons to dust, carried out by Mr. H. L. Green and Mr. H. H. Watson of the chemical defense experimental station, who were lent by the war office for the purpose, the instrument was developed and perfected until it reached such efficiency that all particles likely to be of pathogenic importance could be collected. The investigations are part of the program of the committee on industrial pulmonary disease, which was set up by the Medical Research Council in 1930. In the report it is stated that definite conclusions have been reached that it is undesirable for stone masons to work in closed yards, that on calm days the exposure to dust may be three or more times greater than on a windy day, and that punching (shearing off large quantities of stone by heavy blows on a pointed tool) may account for about half the dust that the mason may inhale. The best preventive measures are the wearing of respirators and brushing the stone free from accumulated dust.

Road Accidents

A table just issued by the minister of transport shows that, in the seven years 1928-1934, 24,385 pedestrians were killed and 533,489 injured; 7,235 bicyclists were killed and 292,098 injured; 16,422 motorists were killed and 545,463 injured. The complete total for the seven years is 48,042 killed and 1,371,050 injured, giving an average of 555 killed and injured every twenty-four hours. For the present year the average so far is 116 killed and 4,016 injured per week. During the seven years the number of killed and injured has been constantly rising—from 170,976 in 1928 to 238,946 in 1934. If the figure is taken as 100 for 1928, the figures for the following years are 103.9, 108.3, 122.1, 124.6, 130.7 and 139.8. The increase for bicyclists is particularly high: taking 1928 as 100, the figure in 1934 was 244.1. The increase of accidents cannot be attributed entirely to increase of automobile traffic, which rose from 2,052,539 vehicles in 1928 to 2,416,908 in 1934. This gives a percentage increase only about half of that for the accidents. The road figures contrast unfavorably with those of train accidents. The number of passengers killed while traveling on railways in 1934 was 17, being one in 96 million.

ACCIDENTS TO CHILDREN

During the present year 500 children have already been killed in road accidents; 103 were cycling. Of 386 killed while on foot, 293 were between the ages of 2 and 9 years. In thirty-two cases children were killed when they escaped from their elders, who were supposed to be in charge of them. There were twenty-two cases of stealing rides and fourteen of chasing a ball into the roadway. Most of the children had been repeatedly warned of the dangers of the roads. The report to the National Safety First Association on the subject states that greater foresight on the part of drivers and closer supervision on the part of parents and others are essential if there is to be any improvement. There were twenty-seven cases in which children were run over when a vehicle restarted or reversed after a stop and the driver failed to notice the child. Older children should be given more "safe-cycling instruction"; also, it is not wise to teach children to "cross quickly," as it tends to make them run across the road—a dominant factor in their accidents. The report also suggests that fatal road accidents to children might be specially investigated by experts with the same thoroughness as accidents on railways.

A School Sanatorium for Tuberculous Boys

At Frimley, Surrey, a new experiment in the treatment of tuberculosis is being carried out at what is known as the Borough Hill Sanatorium Colony, which is a school for tuberculous boys between the ages of 13 and 19. The Borough Hill Colony, founded in 1929, has already proved so successful as to warrant imitation. Seventy per cent of the boys admitted have found employment and some have gained successes at examinations that would be a credit to a normal school. During the last four years 100 per cent passes have been obtained. The boys live under strict discipline and the control of two physicians. They rise at 7 and have their temperatures taken, breakfast at 8 and at 9 go to the classroom or garden. At 12 they rest. At 1:15 they rest again in their cubicles. At 2 they return to the classroom or garden and at 4 knock off for the day and have their temperatures taken again. At 5 there is another period of rest before tea at 5:30. At 6 there is recreation of a kind graded to their state of convalescence and at 8:45 they go to bed. The school has a model office equipped with typewriters and filing cabinets for training for clerkships. Many acres of the grounds are devoted to gardening, for which occupation many of the boys train. The average time taken

to effect a cure is two and one-fourth years. Of 130 patients discharged, thirty-seven obtained posts as clerks and twenty-six as gardeners, thirty-eight obtained other employment, and only fourteen were unable to obtain employment. Eleven were discharged unfit for work. Boys who would have died or who after cure would have been thrown helplessly on the world are returned to society after a few years to lead healthy, useful lives.

Paying Patients in Voluntary Hospitals

The voluntary hospitals (hospitals supported by the voluntary subscriptions of the charitable) were established for the gratuitous treatment of the poor; many patients, however, who do not come under the designation of "poor" cannot afford the cost of private treatment but can pay for treatment in hospitals at charges proportionate to their means. Also there are now numerous methods of diagnosis and treatment that cannot be provided without the aid of the specialized equipment and staff of a hospital except at great expense, if at all. Hospitals that might wish to provide for such persons are prevented by legal obstacles arising from the fact that the need was not foreseen when the legal definition of the hospital was settled. A bill to enable them to do so has been introduced into the house of lords. It provides a uniform method of removing these legal obstacles and at the same time safeguards the interests of the sick poor.

The Falling Birth Rate

In the *Times*, Mr. Robert Rankin, M.P., deplores the falling birth rate and says that there is not enough of British stock to quarter fill the empty spaces of the empire. Australia, for example, has a habitable rainfall area of 1,725,000 square miles, which should hold at the present density of the United States 46,000,000 persons, whereas it has only 6,700,000. Up to 1930 the British dominions had a rate of expansion that would double their population every thirty-five years. Now immigration is at a standstill and the birth rate is declining. In Australia the fall has been precipitate, the annual rate of natural increase having sunk from 17.4 per thousand in 1914 to 14.34 in 1921-1925 and 7.1 in 1934, and it cannot be assumed that it has yet touched bottom.

Mr. Rankin thinks that something should be done to stimulate the growth of population, as has been done in Germany, and, he might have added, Italy. But, like most politicians, he does not fully face either causes or consequences. One of the causes of the decline of the birth rate is industrial depression and unemployment. This in its turn is due largely to political interference in industry and in commerce. The interference of trade unions and, to a less extent, of tariffs has arrested the commercial development of Australia, and its "empty spaces," so deplored by politicians, remain. Mr. Rankin does not tell how to remedy this.

A New Campaign for Road Safety

A new edition of the highway code, which takes the place of the pamphlet formerly circulated only to motorists, has been distributed by the government to every house in Great Britain. In a foreword the minister of transport says: "This code is put in your hands in the sincere hope that the observance of its provisions will make the roads safer. Its provisions are a simple summary of the best and widest experience, each one written in the resolute desire to prevent that kind of mistake or thoughtless action which may result in bereavement or suffering." All together, 15 million copies are to be distributed, of which 80,000 will be in Welsh. The new campaign for road safety is to include a film for motion picture theaters, and a van will visit the seaside resorts and relay the provisions of the code and phonograph talks by the minister and others. Posters in underground stations and in omnibuses in London and in public service vehicles throughout the country will also be used. Large stores, catering firms and others are cooperating in the campaign.

PARIS

(From Our Regular Correspondent)

Aug. 5, 1935.

Suppression of Street and Radio Noise in Paris

The prefect of police of the department of the Seine, in which Paris is situated, some time ago ordered all honking of automobile horns to cease between 11 p. m. and 7 a. m. Recently, these hours have been changed to 9 p. m. and 8 a. m. Perhaps in the near future an effort will be made to imitate the example of Rome, where no honking is permitted at any hour of the day or night. The chief sources of street noise in Paris have been the automobiles, motorcycles, street singers, garbage collectors and pedlers. To these now one can add the radio fans who insist on leaving windows open so that their sound amplifying devices will give the neighbors the benefit of the various broadcasts or records. The Paris police are planning to organize a special antinoise squad, which is to make the rounds of the city so that on receipt of a single complaint the offenders will be warned. If they continue to offend, a police court summons will follow. French radio stations will be asked to participate in the campaign with broadcasts calculated to convince radio fans that they can obtain better results, without disturbing their neighbors, by moderating the power of their sets. As soon as an effective silencer for motorcycles can be found, it will be made obligatory. Any one who has been awakened at 6:30 by the slinging of garbage cans on cement sidewalks will appreciate the order to garbage collectors to perform their task as quietly as possible. Street singing will be limited to those whose cases prove to be worthy and not allowed at an hour when sleep should replace the effort to drown out "harmony murder."

Results of Artificial Pneumothorax for Tuberculosis During Pregnancy

At the May 14 meeting of the Académie de médecine, Rist and Jottras reported their results in the treatment of tuberculous pregnant patients at the Baudelocque Maternity (Professor Couvelaire). The 138 cases included in the report were divided into two groups. In the first there were fifty-eight women in whom the pneumothorax preceded the pregnancy. In the second group were seventy-four in whom this method of treatment was employed during the pregnancy. In the first group, pregnancy occurred while under treatment five years before the report was made, so that one could better judge the end results. Thirty-nine of the fifty-eight in this first group had begun the treatment. Twenty-six, or 67 per cent, of the thirty-nine can be considered cured after five years of observation. Of nineteen women whose pregnancy began less than a year after the pneumothorax treatment, twelve (53 per cent) are cured, three years or more after parturition in the case of nine of the twelve, and two years for the other three. In fifteen women in whom pregnancy occurred at a period when the pulmonary lesions were latent, there were thirteen (87 per cent) cures.

In the second group, of seventy-four cases, in which the pneumothorax treatment was begun during the pregnancy, there were thirty-three (45 per cent) favorable results. The earlier in the pregnancy the treatment was employed, the better was the prognosis, as shown by comparing the 67 per cent of cures in the first with the 45 per cent of cures in the second group.

If one groups the cases according to whether they showed clinical evidence of pulmonary tuberculosis before or during pregnancy, it is to be seen that, of thirty-eight who became pregnant while under treatment, nineteen, or 50 per cent, are cured. On the other hand, in thirty-six women in whom the disease appeared during pregnancy, the pneumothorax has cured only fourteen, or 39 per cent. The latter figure emphasizes

the gravity of tuberculosis occurring during pregnancy. Pneumothorax treatment enables one to save the life of both the mother and the child. Its efficacy will more and more limit the indications for therapeutic abortion in the future.

Popularization of Medicine

A plea to the medical profession to enlighten the public as to recent advances is made by R. Massart in the July 14 *Concours médical*. The article is in line with the publication by the American Medical Association of such a journal as *Hygeia* and the broadcasting program undertaken by the Association. Massart states that the public is often surprised that greater efforts are not being made to keep it informed concerning newer methods of treatment in such a manner that one may keep abreast of medical progress and thus avoid being obliged to secure such information in nonmedical publications. Often all the public, at least in France, knows is what it learns through advertisements of quacks in lay journals. There is much less restriction of this class of publicity here than in the United States. One charlatan in Paris treats all cases by pressure on the sympathetic nerve endings in the nose and his practice can well be envied by those who do not advertise. The public ought to be told that such extravagant claims are impossible to achieve but that the charlatan is profiting by the remarkable success of operations on the sympathetic nervous system by Leriche and other surgeons in France. The patient of the present day is no longer content with the explanations given by the medical man in the past. The higher up in the social and intellectual scale, the more questions are asked by the patient. In France there are journals such as *Guérir* (to cure) which appear weekly and attempt to diffuse knowledge concerning medical achievements, such as the progress made in the treatment of cancer, tuberculosis and heart disease. The articles treat these questions in the simplest nontechnical manner possible, but all criticism and reservations are omitted. The articles are well illustrated. The readers follow the fantastic descriptions as closely as they would an exciting novel, but they cannot distinguish what has been proved and accepted from that which is still in the nebulous stage.

Advice as to treatment can be had from these journals for the asking. This sort of publicity does more harm than good to the medical profession. Advertising campaigns for the use of particular methods have been begun by these lay journals and no one can prophesy how far such a campaign will lead. Massart believes that suppression of these lay publications is impossible. The only remedy is to have the medical profession publish a journal so that in an unselfish manner the duties and the difficulties of the profession can be pointed out. Such a journal should be as well illustrated as are the best of the nonmedical publications. The public should be kept abreast of discoveries in medicine, properly evaluated. The danger of improper and dishonest application by quacks of new methods of treatment must be pointed out. Massart believes his idea is new but evidently he does not know of the excellent work being done in this field by the American Medical Association.

Culture of Entire Thyroid Glands

At the June 26 meeting of the Academy of Sciences, Alexis Carrel and Charles A. Lindbergh made a report of experimental work by which an entire organ or region of the body may be transplanted into a sterile receptacle and through the automatic supplying of a nutrient fluid through the arteries of the organ the circulation may be maintained as under normal conditions. The survival of organs such as the thyroid and ovary has been followed by their development. Such complete visceral cultures is not meant to supplant tissue culture. It differs from the latter not only from the standpoint of technic but also in its objectives. Organ culture aims to study associations of cells and not the latter alone. The complete organ culture is of aid in the observation of the elaboration in vitro of the secretions of endocrine glands, of the substances essential to their growth, of their functional activity, of the laws of association and, finally, of the treatment in vitro of organic and arterial diseases.

The method employed in the study of six thyroid glands of the cat and nine of the rooster was described in detail. Three culture mediums were utilized, blood serum more or less diluted, an artificial medium containing amino acids, and a third containing peptones. The circulation of the first two is accompanied by a diminution in the size of the glands, which, however, conserve their normal structure in part and the follicles remain filled with colloid substance even after twenty-one days of blood serum circulation. The glands undergo degenerative changes in a medium containing relatively high percentages of amino acids. The liquid the use of which is followed by the most marked growth of the thyroid is that containing peptones. In three or four days the gland doubles in size. From the histologic point of view one notes either epithelial proliferation with disappearance of colloid material or an increase in the size of the cells with production of colloid material. There can be no doubt that the gland continues to function, but the architecture, follicular structure and activity vary according to the chemical, physical and physicochemical composition of the fluid circulating through the vessels of the gland. This new method would seem to have important application in physiologic chemistry, pathology and clinical medicine.

Destruction of Rats in Warehouses

The destruction of rats has been studied for many years by Loir of Havre, because of the losses incurred as the result of the presence of rats in the warehouses of this port. At present, only poisons and viruses are employed in France. When a few rats have been killed the colony migrates, but it returns as soon as danger ceases. The majority of rats killed are males (131 out of 140 in one week); hence the reestablished colony does not diminish in number. Loir maintains that cats are the most efficacious agents against the rat menace in seaports. It is unnecessary to attempt to breed a special rat-catching cat. All that will take care of itself, because if the cats are protected and well fed they soon become powerful enough to attack rats. Loir did not belittle the value of bull-terriers but thought their usefulness was lessened by the fact that the rats hear the noise made by dogs, whereas cats work much more quietly. The smaller the number of cats in a given space, the better the results. In Italy, when Mussolini ordered the drainage of the marshy regions near Rome, 3,000 cats were brought to destroy the rats so that they would not interfere with the raising of grain on the drained soil.

An Old Paris Hospital to Be Razed

A final gathering of notables in the Paris medical world was held in May at the Charité Hospital prior to turning it over to the contractors who are tearing the historic structure down. It will be replaced by laboratory buildings of the medical school. Thus disappears the first building in which courses in medicine were given in the eighteenth century. The hospital was founded in 1602 by a religious order, the Brothers of St. John, with the aid of Queen Marie of Medici, wife of Henry the Fourth. At that time Paris possessed only one other hospital, the Hôtel Dieu. Buildings were added from time to time until in 1788 its capacity was 208 beds, arranged in large wards so that medical were separated from surgical cases.

The institution was particularly renowned for its lithotomists, especially Frère Jacques, who is shown in a painting dating back to 1697 surrounded by physicians and removing a vesical calculus through the perineal route. His mortality was so high that he was obliged to leave France.

Desault was a surgeon and Corvisart an internist at the Charité, when in 1789 they held clinics for the first time in French history.

Among other famous medical men who had services during the nineteenth century may be mentioned Potain and Laënnec.

The famous amphitheater in which Corvisart taught pathology has been visited by thousands of physicians from foreign countries.

The *Paris médical* devotes its August 3 issue to the history of this famous institution, and the illustrations show all the stages of its development and the part the Charité has played in French medicine.

Alcohol Injections of Phrenic Nerves in Bronchiectasis

At the May 10 meeting of the Société médicale des hôpitaux, Chiray and Malinsky reported a case of cylindric dilatation of the bronchi with profuse purulent expectoration and high temperatures which did not improve during a month's stay in the hospital. Alcohol was then injected into the left and a few days later into the right phrenic nerve, to inhibit the movements of the corresponding halves of the diaphragm. The inhibition was verified by radioscopy. This treatment was followed by marked improvement in the amount of expectoration. Injection of the bronchi with iodized oil and subsequent radiography revealed bronchi of almost normal size. The patient can be considered clinically cured.

In the discussion, Rist stated that he had advocated phrenicectomy ten years previously for dilatation of the bronchi. He had some remarkable results. Rist has never been obliged to operate on both phrenic nerves.

Lereboullet reported a gratifying result in a boy of 9 with congenital bronchiectasis of the left lower lobe, profuse expectoration and clubbed fingers. The profuse expectoration ceased after a phrenicectomy, the diaphragm rising 4 cm. The fingers assumed their normal aspect rapidly. In other children, postural drainage, as advocated by Quincke, had been followed by marked improvement; hence operative treatment would be less often indicated in children.

Sergent believed that alcohol injections are preferable to phrenicectomy. He had never observed any benefit from phrenicectomy in chronic bronchiectases, but it was efficacious in cases following a bronchopneumonia with slow resolution. No single method can be considered as the choice in the treatment of bronchiectasis.

Recovery Following Mercuric Chloride Poisoning

Marchal, Soulie and Grupper reported a case of mercuric chloride poisoning with recovery at the April 12 meeting of the Société médicale des hôpitaux. A woman of 28 swallowed 5 Gm. of corrosive mercuric chloride dissolved in water. Three days later, anuria appeared accompanied by a blood urea of 270 mg. per hundred cubic centimeters, rising later to 535 mg. Following multiple transfusions of from 300 to 350 cc. the anuria, which had lasted twelve days, disappeared, the urinary output attaining as high as 3,500 cc. in twenty-four hours. The alkali reserve of the blood remained about normal throughout. The electrocardiographic changes included flattening of the T wave, inversion of the latter and widening of the ST space, all of which indicated myocardial changes of a toxic character. The blood showed at the beginning a marked polymorphonuclear leukocytosis followed by a late aplastic anemia with progressive granulopenia as indicative of bone marrow involvement. The cardiac condition responded very well to digitalis in large doses. They believe that the blood transfusions and the frequent administration of salt solution to compensate for the loss of chlorides as shown by the blood examination are responsible for the favorable outcome.

BERLIN

(From Our Regular Correspondent)

July 22, 1935.

Training School for Leaders in German Medicine

June 1, on a specially chosen area in a former village of Mecklenburg, in charming scenic surroundings, a training school for leaders (fuehrer) in German medicine was opened with fitting ceremonies. According to the address of Dr. Wagner, the federal fuehrer of the medical profession, the purpose of the school is "to open the mind of the future medical fuehrer to the value and the blessings of the healing forces of nature and its elements. It is designed to help liberate him from the spirit of prejudice and dogmatic intolerance with which he may be inclined to view old school medicine, and to teach him to cooperate in a spirit of camaraderie with all those who, as his co-workers, are laboring to promote the cause of public health." In addition, candidates are expected to secure, through attendance on the organized courses, a knowledge of law, an intimate acquaintance with the mode of functioning of organized society, and a knowledge of the heredobiologic and racial principles governing the new policy of health culture in Germany. During the present summer about 600 local leaders connected with the public health service of the national-socialist party will receive special training in intensive fourteen-day courses. Later on, six weeks' courses for the advanced training of a selected few will be organized.

Mortality from Circulatory Disorders

Disorders of circulation have been for some time the most frequent cause of death. In 1931 Germany's mortality from "diseases of the circulatory organs" and from cerebral hemorrhage amounted to 27.5 per 10,000 of population, which constituted 24.4 per cent of the total mortality. The mortality of diseases of the circulatory organs increases with the age of the patient. From about 1 death per 10,000 in childhood there is an increase to 400 per 10,000 in old age. Conclusions based on the statistics, Dr. Koller of the Kerckhoff Institute for Cardiac Research in Bad Nauheim brought out, are greatly impaired by their varying degree of reliability. More exact collection of statistics on the causes of death usually results in higher mortality rates for the diseases of the circulatory organs. Many cases of "senile weakness," if examined more in detail, would be found to be cases of circulatory disorder, while a somewhat smaller percentage of cases of "heart disease" might be more accurately diagnosed. In Saxony in 1922 about 89 per cent of all deaths ascribed to diseases of the circulatory organs were certified by physicians, as compared with only 81 per cent of the deaths due to all causes. With regard to infants, the reliability of the statistics on the causes of death was low, being estimated at 50 per cent. With the exception of the youngest age group, deaths from diseases of the circulatory organs are certified with reasonable accuracy in the main.

Recent decades have brought a sharp increase in the mortality due to circulatory diseases. One of the main reasons for the increase is the upward shift in the average age of the population —the absolute and the relative increasing percentage of old persons. This explains only a part of the increase; for, in spite of the changes in the numerical representation of the older age groups, the mortality in Prussia from 1905 to 1925 would have increased only to 22.3 for men and to 20.8 for women, and in Bavaria, during the period from 1900-1901 to 1925, to 23.0 for men and to 24.0 for women. The actual increase, however, is much greater, so that only 88 and 44 per cent, respectively, of the increase in Prussia from 1905 to 1925, and 48 and 26 per cent, respectively, of the increase in Bavaria during this period may be explained by the shifting that has occurred in the population. The increase among the men is greater than

for the women. The difference is caused by the greater number of men who lost their lives in the World War, which increased the relative representation of the older age groups. Whether any other factors besides shifting in the relative representation of the age groups and improvements in diagnosis have contributed to the increased mortality from diseases of the circulatory organs appears doubtful.

While the mortality from diseases of the circulatory organs has increased in the older age groups, it shows a distinct decline in the younger and the middle groups. Here too an improvement in the quality of the statistics will play a part, chiefly through the turning over of a number of deaths to the brackets of various infectious diseases, as the fundamental disorders. It is quite possible that part of the reduction in mortality of the young is explainable by better therapeutic results. In infants, conditions are different. The improved classification of causes of death brought usually (particularly in Prussia) a marked decline in the figures for infants. In Bavaria, however, the figures show an increase. The influence of the seasons on women is greater than on men. Persons of advanced age are more affected by the seasons than persons of the middle and the younger group. The course of the curve appears to justify the assumption that the increased mortality of the winter is due to the premature termination of a number of lives that would have continued only a few months longer at best, and that the reduced mortality of the following summer is in the nature of a compensatory adjustment. If this assumption is true, a high winter peak would be followed by an exceptionally low summer mortality. A scrutiny of the statistics, however, revealed that, aside from the fact that the winter and the summer curves may reflect a common increase, the curves have no connection; the winter and the summer figures show a wide fluctuation independently of each other. The increased mortality of the winter does not therefore concern persons with an especially unfavorable prognosis. There appears to be no doubt that the winter's additional toll of diseases of the respiratory organs plays a part. It is well known that, associated with periods of influenza, deaths from diseases of the circulatory organs show an immediate and marked increase. The greater menace to persons with disorders of the circulatory organs that accrues from the more frequent complications of winter does not, however, explain entirely the seasonal differences. This is shown by a comparison of the weekly statistics of Germany's large cities for the winters of 1932-1933 and 1933-1934. In both years the winter peak for diseases of the circulatory organs reached a height hardly explainable by chance. In the winter of 1932-1933 the upward trend coincided with the wave of influenza. In the winter of 1933-1934, however, the influenza wave was not associated with any marked rise, so that other factors during this winter period must have influenced the high mortality from diseases of the circulatory organs.

Stomach Ulcer and the Kymogram

In roentgenologic examination of the stomach the use of the kymographic method is by no means a substitute for fluoroscopy or the ordinary film, as Cramer pointed out in a recent address before the Berlin Medical Society. Kymography, however, serves a special purpose—namely, the demonstration of a simple ulcer even though a tumor of the mucous membrane is absent. This is made possible owing to the fact that with the kymograph the functioning of the stomach, including the peristaltic waves, may be studied. Several important data have been discovered. Evacuation of the food from the stomach is not accomplished by peristalsis but rather by contraction of the stomach. During the contraction the food is pressed downward through the pylorus and upward toward the cardia. Likewise the lesser curvature executes peristaltic movements, although of a slighter degree. In the presence of an ulcer, a typical manifestation is the general hyperperistalsis of the whole stomach in contrast with the dynamic rigidity in the immediate vicinity of the ulcer. From this "aperistaltic" zone one can diagnose kymographically a simpler ulcer; also a bleeding ulcer. In extraventricular tumors, the kymogram was found useful also in establishing a differential diagnosis.

Medical Advisers in Shoe Establishments

For years, ethical German physicians have strongly deprecated the custom of large shoe establishments engaging physicians to serve as expert advisers to their customers in the purchase of suitable shoes. In this manner alleged orthopedic shoes were disposed of that did not meet the requirements of orthopedists. The medical court of honor for the Berlin district has now rendered a decision to the effect that physicians are prohibited from serving as medical advisers in shoe establishments. The physicians who have been serving in that capacity have been notified that they must terminate their contracts with shoe firms at the earliest possible moment. All physicians working under such contracts who do not announce within a few days their compliance with the law will be reported to the court of honor.

Industrial Accidents in 1933

Government authorities and private organizations are constantly calling attention to the menace of industrial accidents. In the official Nachrichten für Reichsversicherung, statistics were recently published showing that in 1933 in the industrial plants included in the "gewerbliche Berufsgenossenschaften" 427,688 accidents occurred, 2,402 of which resulted fatally. In 1932 there were 461,682 industrial accidents, 2,311 of which proved fatal. The increase is due chiefly to the fact that the number of plants rose from 1,124,848 in 1932 to 1,145,026 in 1933, while the number of persons insured mounted from 8,280,075 in 1932 to 8,977,155 in 1933. As compared with 1913, the number of industrial accidents was 53,523, or 9.21 per cent lower, while the number of insured was 15.5 per cent less. The maximal number of industrial accidents during recent years occurred in 1928, there having been 1,046,112 accidents with 5,252 fatalities.

Although the number of accidents compared with 1932 shows an increase, which is due to a great extent to the enrolment of a large number of unskilled workmen, it may be noted that the number of persons receiving accident compensation for the first time has declined by 4,554, or 14.37 per cent. Without doubt this good showing is the immediate result of accident prevention propaganda.

Decline in Suicide Rate

The statistical bureau of the city of Berlin has published a series of statistics on suicide in Berlin in relation to unemployment, during the decade 1925-1934. An examination reveals that the two curves show a surprising resemblance. When the unemployment increases, the suicides increase, although not to the same extent. When, during the years 1925 and 1926, the number of unemployed mounted rapidly (from 81,000 to 275,000), the suicides increased from 1,587 to 1,779. In 1927, when the unemployed in Berlin dropped to 209,000, the suicides declined to 1,687. The same observation was made in 1928, the number of unemployed numbering 183,000 and the number of suicides 1,481. Since 1928, unemployment has increased steadily and likewise the number of suicides. In 1932 the maximum was reached, the statistics showing 635,000 unemployed and 2,262 suicides. In 1933 the number of unemployed dropped to 611,000 and at the same time (and in almost the same proportion) the number of suicides fell to 2,136. In 1934 there were 417,000 unemployed and 1,811 suicides. As former observations have shown, it is evident that the suicide rate is strongly influenced by economic conditions.

ITALY

(From Our Regular Correspondent)

July 15, 1935.

International Congress of Hospitals

The fourth International Congress of Hospitals, organized by a committee on which the Spanish prefect served as chairman, was held recently in Rome. The first topic, which was covered by four speakers, was "The Hospital from the Standpoint of Public Health."

The first speaker, Professor Ronzani, director of the Hygienic Institute of the University of Milan, developed the subject from the point of view of general hygiene and demonstrated the need of coordinating the existing hospitals, by province or region, with relation to their equipment. He proposed the creation of provincial committees, whose duty it would be to coordinate the hospitals and promote the construction of new hospitals or the reorganization of existing institutions in accordance with the technical and hygienic standards established by the ministry having jurisdiction. In every hospital should be established consultation centers for the early diagnosis of disease and for the treatment of patients dismissed from the hospital proper. The program would be completed by the creation of professional schools for nurses and for hospital social workers. The latter would serve as mediators between the physicians, the welfare organizations, the insurance companies and other bureaus.

The second speaker, Dr. Browne of Scotland, treated the problem from the point of view of social hygiene and political economy. He emphasized that the constantly increasing number of patients makes necessary an increase in hospital services, which might become effective centers of public hygiene. The difficulties in the way of improvement in hospital services are due to the lack of a rational classification of patients, to defects of construction and equipment, and to an inadequate personnel.

The third speaker, Professor Rüdin of Germany, discussed the eugenic problem, pointing out that the activities of the hospitals in this field must be controlled by the central government, and that hence it is necessary for hospital physicians to know the scientific bases of eugenics, which is founded on the preservation of the health of the race, which includes protection against hereditary taints. The hospitals may render useful service by publishing detailed statements on hereditary diseases.

Hospital physicians should not confine themselves to collecting information on the patient but should extend their investigations to the members of his family.

The fourth speaker, Professor Sarraz-Bournet of France, took up the administrative side, and contended that the hospital should not be solely an institution for the treatment of patients but should also participate in social work, introducing, among other things, courses in sanitary instruction.

The second topic, "The Organization and the Technical Installations of Hospitals," was discussed by speakers representing respectively the United States, Poland and Switzerland. The first speaker, Schwitalla, spoke on the coordination of hospital activities to improve the quality of the aid rendered patients, and expressed his regret that at present there are too many organizations in this field, while a fixed purpose is lacking. The work of the physicians, the nurses, the administrators and the various welfare organizations should be subordinated to the chief aim of the hospital—namely, furnishing the patient with the best care possible.

The second speaker, Professor Mogihnicki, spoke on the economic principles that should govern the technical organization of a hospital, emphasizing that all luxury should be suppressed and only those things done that improve the quality of the services.

Professor Van der Leen of the Netherlands explained a system of bookkeeping especially applicable to hospitals.

The question of eugenic sterilization was then taken up and gave rise to animated discussions. Dr. Schultze of Germany emphasized that the modern hospital, in addition to the positive task of restoring the patient to health and strength, must assume also a negative task, which consists in depriving of procreative power such patients as are affected with hereditary taints. In the opinion of the speaker, the regulations at present in force in Germany will be adopted by all civilized countries. This view was frankly opposed by Dr. Doherty of Ireland and Dr. Groonenberg of Amsterdam, who protested in the name of the Netherlands delegation. Likewise Professor Lépine of France declared that the problems of eugenics and of sterilization should be banished from congresses on hospital management, since the duty of the hospital is to promote the treatment of sick persons.

Tuberculosis of the Bones and Joints

Under the chairmanship of Professor Putti, the second congress for the study of osteo-articular tuberculosis was held recently. The first topic was "Internal Localizations of Osteo-Articular Tuberculosis in the Child." The opening paper was presented by Professor Frontali, who emphasized that osteo-arthropathy in the child is due in 84 per cent of the cases not to bovine tubercle bacilli, as has been contended by some, but to human bacilli, the first localizations of which are commonly found in the respiratory system. The speaker held that the diffusion of the tuberculous virus takes place from foci—usually intrathoracic—by way of the blood, giving rise to localizations also in the skin, which are frequent in children with osteo-articular involvement. Contrary to the general belief, children affected with tuberculous osteo-arthropathy may spread contagion among children with whom they associate, because of localizations in the respiratory tract that are often overlooked. Sometimes the pulmonary focus exerts a decisive influence on the outcome of the orthopedic treatment. He opposed the conception of Marfan that osteo-articular tuberculosis furnishes increased resistance to pulmonary infection and demonstrated that tuberculous spondylitis, for example, gives rise to mechanical conditions that favor the evolution of pulmonary disorders.

The second topic was "Radiodiagnosis of Osteo-Articular Tuberculosis," which was opened with a paper by Professor Zanoli. He considered atrophy, which is neither characteristic nor constant in tuberculosis. In fact, many other pathologic conditions are associated with atrophy. Osteosclerosis and osteophytic growths are more frequent than is supposed. The age of the patient is important in explaining the diverse behavior. Periostitis ossificans and diaphyseal localizations are characteristic of early years. The destructive phenomena are more frequent in the child than in aged persons, in whom the lesions are more circumscribed. There are diagnostic difficulties; for example, the radiographic interpretation of a cervical lesion is difficult, since, in the majority of cases, the more positive the roentgenogram is, the more certain it is a lesion in a reparative stage. The observations are uncertain also in sacrocoxitis, which becomes manifest only when there are extensive lesions; the same may be said of costal and sternal caries. In tibiotarsal tuberculosis the evolution is similar to that observed in the knee. It is not clear why tuberculosis of the hip manifests itself nearly always in the form of destructive phenomena, whereas in the knee and in the foot these are much less frequent. In general, the pathologic condition revealed by the roentgenogram appears to be less than it really is. Furthermore, roentgenograms are negative with respect to abscesses, except mediastinal, calcareous and occasionally psoas abscesses. Finally, diagnostic difficulties arise in the differentiation of syphilis from osteomyelitis. While the speaker admits that radiology has great merits, he concludes that the patient must be studied and judged chiefly by clinical aids.

Verdina spoke on the value of Meinicke's new serodiagnostic test for tuberculosis. The test is technically and biologically

similar to that proposed for syphilis, by the same author. In a series of 205 cases, the speaker secured only negative reactions in healthy persons. In persons known to be tuberculous he obtained 85 per cent of positive, 13 per cent of doubtful and 2 per cent of negative results.

RIO DE JANEIRO

(From Our Regular Correspondent)

July 15, 1935.

Treatment of Cutaneous American Leishmaniosis with Sodium Arsenite

Dr. Aguiar Pupo, director of the department of skin diseases of Santa Casa, a hospital for women in São Paulo, recently read, before the Sociedade de Medicina e Cirurgia of São Paulo, a preliminary report on the results of the injections of sodium arsenite in the treatment of cutaneous American leishmaniosis. The author has obtained satisfactory results, from January of the present year up to now, from the injections of sodium arsenite, prepared by the following formula:

Arsenic trioxide	
Neutral sodium carbonate	0.25 Gm.
Sodium chloride	2.00 Gm.
Distilled water	250 cc.

The solution is placed in ampules of 2 cc. and 5 cc. capacity and sterilized. A cubic centimeter of the solution contains a milligram of sodium arsenite. The injections are given twice a week intramuscularly, beginning with 2 cc. and increasing it after the first two weeks until 5 cc. at each injection is reached. Improvement of the ulcerations is noticeable after the second week of treatment. By the end of the treatment, which lasts for thirty or forty-five days, the ulcers as a rule are entirely healed. The injections are well tolerated by the patients. The pain during the injection is slight and no local inflammatory reaction occurs. Some patients react with stomachache or headache, which lasts all the first day. The reaction is controlled either by reducing the dose or by increasing the interval between the injections. The treatment, in comparison with the administration of antimony and arsenical preparations, has the advantages of the use of sodium arsenite, a drug accepted by the international pharmacopeias, the simple technic for preparation and administration of the injections and the moderate expense. The specific action of arsenic trioxide and of its alkaline salts on certain organisms is proved by the results reported in the treatment of experimental trypanosomiasis, of cutaneous American leishmaniosis reported by the speaker, and of malaria, previously reported by Slevogt and Frieck of Germany (1700-1710), by Fowler, Frei, Wilan and Pearson of England (1786), by Boudin of France (1842) and more recently by Brera, Tommasi, Crudelli and Richi of Italy.

Encephalography in Schizophrenia

Drs. Fausto Guerner, J. Fajard, M. Jahn and Celso P. da Silva in a lecture recently delivered before the Sociedade de Medicina e Cirurgia of São Paulo reported the results of suboccipital injections of air in the treatment of schizophrenia at Juquery Hospital. The work of the speakers was based on that previously reported by Jacob and Jinkler, Jacobi, Moore, Nathan, Elliott and Laubach Foster. The age of the patients, four women and four men, ranged between 19 and 52. In the majority of the patients the mental condition was not complicated by any other disease. The mental disturbance had developed long before in two patients, recently in one, and it had been of moderate duration in five. The quantity of cerebrospinal fluid removed, prior to the injection of air, was 45, 80, 90, 110, 110, 125, 130 and 140 cc. The quantity of air injected was equal to that of cerebrospinal fluid removed in three cases and from 10 to 15 cc. less than that in five cases. For the interpretation of the results the criterion established by the American Committee for Standardization of Encephalographies was followed; that is, the comparison of the encephalograms of schizophrenic patients with those obtained from patients with other diseases and from normal persons. The speakers conclude that: The presence of atrophy of the frontoparieto-occipital zone of the cerebral cortex was detected by encephalography in a group of eight schizophrenic patients, intense in seven and moderate in one. The frontoparieto-occipital zone and more intensely the upper parietal lobulus were involved in cases of intense atrophy. Only the upper parietal lobulus was involved in the cases of moderate atrophy. There was ventricular dilatation in three cases, intense in two and moderate in one. The size of the cisterna basalis was much increased in three cases and moderately increased in two. The most advanced pathologic changes were seen in the two cases in which the disease had developed long before. Cortical atrophy was seen even in the case of more recent development, about one year, during a remission of the condition.

Virus in Trachomatous Tissue

Dr. A. Busacca recently reported to the Sociedade de Biologia of São Paulo that he obtained the development of trachomatous nodules in the choroids and the ciliary body of rabbits and chickens by the inoculation of fragments of tissues from human trachomatous eyes that have been kept in the icebox in 50 per cent glycerin from eight or fifteen days and then inoculated in the vitreous body of the animals. The material from the trachomatous nodules of the eyes of the animals was kept in glycerin for five days and then inoculated in the vitreous body of rabbits and chickens in a new lot, in order to obtain serial transmission of the virus. The development of trachomatous nodules has been proved by the histologic examination of the eyes of the animals up to the second serial transmission. The period of development of the nodules is about forty-five days after the inoculation of trachomatous tissues.

JAPAN

(From Our Regular Correspondent)

July 3, 1935.

Measures to Combat Tuberculosis

The board of health is making efforts to combat tuberculosis under a ten-year plan. The first thing is to establish a "health center" in every city and town. At present there are only 115 health centers in the country. Practitioners will be obliged to report to this center the names and addresses and other necessary data about patients with tuberculosis. This compulsory report to the authorities was at first opposed by physicians on the ground of professional secrecy. The health center, however, will be in charge of medical officers; consequently, the patients' data will always be kept among physicians. The center will chiefly work for the early examination of suspects and the prevention of tuberculosis. The physicians at the center will first cooperate with the primary school teachers in finding tuberculous school children.

On the other hand, the board of health will soon give orders to schools, factories, dormitories, theaters, department stores and buildings where numbers of people assemble to the effect that they should have more sanitary equipment for combating this disease. Indigent patients and members of their families will be given aid.

The sickness insurance, which is also under the control of the home office, has decided to give a physical examination to any applicant from any factory that has joined the sickness insurance. At least twice a year, all employees will be examined. The panel physicians are required to report every person sick with tuberculosis.

One of the most urgent needs is to spread knowledge of the danger of tuberculosis among the people. The board is planning to hold an exposition in every large city.

The war office, which is obliged to invalid out of the army any tuberculous soldier, is reported to have planned a new measure to solve its problem. It will help the families of the invalided soldiers with money if possible.

The education office has put its hand to combating tuberculosis in teachers in primary schools. The new plan is to have a sanatorium in each of the fifty-six prefectures within the coming ten years. The initial expenses will be paid in part by the government and in part by the mutual aid association of the teachers organized in every locality; the rest will be paid by the local government. The cost of administration will be paid by the local government and by the association. In some prefectures this system is already working on a small scale.

Annual Examination of Primary School Children in Tokyo

The physical examination of all school children in the capital was recently done for this year. Those examined comprised 344,448 boys and 332,139 girls between 7 and 15 years of age in the primary schools; 56,710 children were found to be near sighted and 2,135 astigmatic; 26,964 suffered from trachoma and 5,756 from color-blindness; 3,585 children had some defects of hearing. Those who had inflammation or enlargement of the cervical glands amounted to 28,413, enlarged tonsils 132,768 and favus 35,064.

Dr. Kanasugi Honored

The celebration of Dr. Eigoro Kanasugi's seventieth birthday took place June 22 in Tokyo under the auspices of the Japan Medical Association. He is a member of the house of peers and an influential politician as well as an expert nose and throat specialist with a large hospital in Tokyo. On this occasion more than 600 prominent personages were present, including the prime minister and three other cabinet ministers. It was the most successful meeting held in several years. He was given an offering of 10,000 yen collected from the members of the Japan Medical Association in recognition of his services to medicine in this country and to the public. A bronze bust will be erected in front of the office of the association. He declared that he would retire from medical practice and politics, although he is now greatly needed when medicine has many important questions to be solved. He will remain as the president of the Jikei Medical College.

Prostitution in Japan

The unlicensed prostitutes throughout the country who were arrested in 1933 on the charge of being a social menace numbered 6,642, and numerous others escaped arrest. Of these, 6,374 were examined and 223 were found to be suffering from syphilis, 903 from gonorrhea, 209 from soft chancre and 134 from other venereal diseases. Of the licensed prostitutes, 49,302 were distributed among 509 licensed quarters, under the charge of 10,281 brothel keepers. The number of pleasure seekers who visited those prostitutes in 1933 was 24,922,504, a great increase as compared with previous years. The "geisha girls," who play the part of bar-maid, singer, waitress and sometimes prostitute if required, though unlicensed, numbered 74,200 throughout the country in 1933. Their numbers are decreasing considerably, owing to the rapid increase of waitresses, but they are more or less a source of venereal diseases.

While the abolition of licensed prostitutes will be carried out in the near future as declared by the government, the prevention of venereal diseases will remain a great social problem, in view of the unlicensed prostitutes. The delay in abolishing the licensed prostitute is due in part to this problem of the unlicensed prostitute.

MOSCOW

(From Our Regular Correspondent)

Aug. 17, 1935.

The Congress of Surgeons

The twenty-third All Union Congress of Surgeons was held in Leningrad, June 25-30. Prof. Nicolas N. Bourdenko of Moscow read a paper on shock, which he considers the sum of reactions to different insults. Experimental shock can be studied in animals. Postoperative shock is much more amenable to study. The diminution of blood circulating in the vessels (as the result of operative intervention) gives a fall of venous pressure and a respective laxity of the work of the right side of the heart. Curative measures must aim at stimulating the vessel-moving center, to augment the total mass of blood taking part in the circulation. In cases of grave losses of blood, transfusion must be used.

A. L. Polenov of Leningrad reported the results of 200 extirpations of cerebral tumors. Prof. Jacob M. Brouskin of Moscow spoke on the organization of anticancer campaigns. About 5,000 cancer patients were hospitalized in the Leningrad Oncologic Institute and twenty city hospitals in the last nine years. This number includes 2,937 cases of cancer of the stomach, 1,249 of the mammary glands, 337 of the rectum, sixty-two of the mouth and 422 of the lip. The third topic of the congress was abscess and gangrene of the lungs. Prof. Serge I. Spasocucozky analyzed 312 cases of this disease that he observed at Moscow in the last eight years. Abscess and gangrene of the lungs were four times more frequent in men than in women. The fourth program topic of the congress was devoted to the evacuation of injured soldiers in military operations. There was read a series of reports by physicians from the Military Medical Academy, about the type of surgical work to be done at different stages of evacuation. The last program reports were devoted to pseudarthrosis. Papers were read by Professors Tourner, Sitenko and Chaklin. The next All-Union Surgical Congress will be held at Moscow in 1937.

The Kazan State Institute

On April 23, 1920, in Kazan, the Clinical Institute for Graduation of Physicians was opened. During the last fifteen years the institute has graduated more than 5,700 physicians. In 1934 the number of graduates was 1,073. A special group of student-managers of district health departments is taught how to organize soviet health care. They study organization, the planning of health care, medical economics, and so on. During the last fifteen years the institute has produced twenty-five professors, thirty-three dozents and 211 assistants. The scientific research work of the institute is closely connected with its practical work. It has resulted in about 2,000 publications printed in the "volumes" of the institute, in the *Kazan Medical Journal* and other medical journals of the Soviet Union and foreign countries. About 10,000 patients are admitted every year by the clinics of the institute. All graduate students in the institute receive a scholarship which equals the salary they obtained when they are on duty. In many towns, especially university centers, institutes for graduation of physicians, as in Kazan, are formed.

Marriage and Divorce

The principal difference between soviet and capitalist legislation on marriage and divorce is that this important act can be done in our country without difficulties of a juridical or religious character. Marriage and divorce in the Soviet Union are much easier than in other countries, yet the population looks upon marriage with gravity. The Central Institute of Mother and Child Care studied 2,000 families of workers at Moscow. The results obtained by the institute are of interest. Before the October revolution, 78 per cent of women married

at an age younger than 20 years and 15.3 per cent married between 21 and 24. After the revolution the corresponding data are 44.4 and 36.6 per cent. The higher level of matrimonial age shows more seriousness about the question of family building. Of the prerevolutionary marriages, 53.9 per cent occurred after one month of acquaintance and 16.5 per cent after three to twelve months. At present the corresponding figure is 20.7 per cent and, after a six months acquaintance, 55.7 per cent. These data show that at present more discretion is observed in contracting a marriage. The number of divorces is higher than before the revolution. The initiative in divorces is taken mostly by the women. These figures show that soviet legislation helps to build a family on a more solid foundation than before the revolution.

The International Congress of Physiologists

The fifteenth International Congress of Physiologists was opened August 9 at Leningrad in the former state douma hall under the presidency of Prof. Ivan Petrovitch Pavlov. About 1,500 delegates from thirty-seven countries were present at the congress, the United States and Great Britain being represented by a delegation of 297 members. Three hundred and six papers were read by foreign guests and 169 by soviet scientists. Twenty-two scientific films were demonstrated. In the laboratories of the military medical academy twenty-four different experiments were demonstrated.

The congress was greeted at the opening meeting by the secretary of the Central Executive Committee of the Union of Socialist Soviet Republics, by the People's Commissar of Health, Kaminsky, and by others. The halls where the meetings of the congress were held have loud speakers arranged so it is possible to hear all the papers simultaneously in five languages—English, Russian, French, German and Italian.

In their leisure time, the delegates visited the town and suburbs, laboratories, clinics and scientific establishments, in particular Pavlov's laboratories at Coltushi near Leningrad. The last plenary meeting of the congress was held at Moscow, August 17. In following letters will be given a report on the scientific work of the congress.

Marriages

CHARLES ROY HOSKINS JR. to Miss Virginia Eubank Segar, both of Saluda, Va., at Washington, D. C., July 1.

THEODORE F. HAMMERMEISTER, New Ulm, Minn., to Mrs. Pearl L. Rexford of Minneapolis, recently.

HUGH M. C. LINDER, Clifton Springs, N. Y., to Miss Eleanor Shelton of Nashville, Tenn., June 15.

RICHARD H. KIENE, Concordia, Kan., to Miss Edith Elizabeth Swing of Bryn Mawr, Pa., June 8.

ALFRED J. SILBIGER, Randolph, Ohio, to Miss Evelyn Cheswick of East Cleveland, June 16.

HAROLD J. KULLMAN, Detroit, to Miss Edna Mary Warner at Cheboygan, Mich., July 13.

ARTHUR B. RICHTER, Flora, Ind., to Miss Lyda Mary Fisher of Steubenville, Ohio, May 7.

SAMUEL R. KAUFMAN to Miss Martha Davidow, both of Wilkes-Barre, Pa., May 2.

NATHAN W. RUBIN to Miss Dorothy M. Moyer, both of Norristown, Pa., April 28.

ROBERT I. MCPHAIL to Miss Helen Bernice Ebersole, both of Arcadia, Ohio., May 10.

GEORGE E. MCGINNIS to Miss Margaret Dager, both of Norristown, Pa., May 4.

ALBERT HAROLD KEEFER, Marquette, Mich., to Miss Ruth Doolittle, June 27.

ADOLPH ALLAN SMOLEN to Miss Mildred Gerber, both of Chicago, July 7.

RUBIN M. LEWIS to Mrs. Elsie Finn, both of Philadelphia, May 21.

Deaths

Edwin P. Sloan ⊕ since 1932 a member of the Judicial Council of the American Medical Association and from 1924 to 1932 a member of the House of Delegates, died, September 13, at his home in Bloomington, Ill., of myocarditis. Dr. Sloan was born in Neosho, Mo., Feb. 13, 1878. He received his medical degree from the University Medical College of Kansas City (Mo.) in 1898 and later studied in Berne, Switzerland, and took graduate work at the University of Berlin, Chicago Polyclinic and the New York Post-Graduate Medical School. From 1898 to 1903 he practiced in Danvers, Ill. In 1905 he settled in Bloomington, where he specialized in the surgical treatment of goiter and diseases of the stomach. He was a founder of the American Association for the Study of Goiter and a former president of that organization. He was a founder also of the International Conference on Goiter in Berne, Switzerland, and several times served as a delegate. He was a member of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons; past president of the Illinois State Medical Society, and past chairman of the advisory board of the Illinois Department of Public Health. Dr. Sloan was surgeon-in-chief of the Sloan Clinic and on the staffs of the Mennonite Hospital and St. Joseph's Hospital. He had written many articles on goiter, abdominal surgery and gynecology and had practically completed the writing of a textbook at the time of his death.

Charles Norris ⊕ New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1892; since 1918 chief medical examiner of New York; professor of forensic medicine, New York University College of Medicine; formerly instructor of pathology and assistant in bacteriology and hygiene at his alma mater, and instructor in pathology of infectious diseases, Cornell University Medical College; member of the American Association of Pathologists and Bacteriologists and the American Society of Clinical Pathologists; director of laboratories at Bellevue Hospital, 1904-1918; was decorated *Chevalier de la Couronne*, Belgium; in 1934 was awarded the gold medal of the New York Academy of Medicine for distinguished service in medicine; was widely known as an expert on medical jurisprudence and was instrumental in the solution of a number of notorious medicolegal cases; aged 67; died, September 11, of coronary sclerosis.

Ross McPherson ⊕ New York; Harvard University Medical School, Boston, 1902; member of the Massachusetts Medical Society and the American Association of Obstetricians, Gynecologists and Abdominal Surgeons; fellow of the American College of Surgeons; professor of gynecology and obstetrics, New York Polyclinic Medical School and Hospital; on the staffs of the United Hospital, Port Chester, Caledonian Hospital, Brooklyn, Dobbs Ferry (N. Y.) Hospital, Long Beach (N. Y.) Hospital, John T. Mather Memorial Hospital, Port Jefferson, N. Y., Hackensack (N. J.) Hospital and the Holy Name Hospital, Teaneck, N. J.; aged 59; died, August 16, of cerebral hemorrhage.

William Walter Lewis ⊕ St. Paul; University of Minnesota Medical School, Minneapolis, 1902; assistant professor of ophthalmology, otology, laryngology and rhinology at his alma mater; member of the American Academy of Ophthalmology and Oto-Laryngology; past president of the Minnesota Academy of Ophthalmology and Oto-Laryngology; fellow of the American College of Surgeons; served during the World War; on the staffs of the Charles T. Miller Hospital, St. Luke's Hospital, St. Joseph's Hospital and the Children's Hospital; aged 59; was found dead in the Mississippi River, July 29.

John Alexander MacIsaac, New York; Harvard University Medical School, Boston, 1896; member of the Medical Society of the State of New York; served during the World War; at one time acting assistant surgeon lieutenant, with rank of junior grade, in the U. S. Navy; fellow of the American College of Surgeons; instructor in otorhinolaryngology, University and Bellevue Hospital Medical College; on the staffs of the Children's Hospital and the New York Eye and Ear Infirmary; aged 61; died, August 16.

Robert Douglas Roller Jr., ⊕ Charleston, W. Va.; University College of Medicine, Richmond, Va., 1905; fellow of the American College of Physicians; served during the World War; past president of the Kanawha County Medical Society; medical director of the Hillcrest Sanatorium; on the staffs of the Charleston General Hospital and St. Francis Hospital; consultant to the Veterans Administration; aged 56; was killed, August 10, in an automobile accident.

Charles Willard Selover ✠ Canandaigua, N. Y.; University of Buffalo School of Medicine, 1904; past president of the Ontario County Medical Society; served during the World War; medical director of the Oak Mount Sanatorium, Holcomb; on the staffs of the Veterans Administration Facility and the Frederick Ferris Thompson Hospital; aged 53; died, July 26, in the Clifton Springs (N. Y.) Sanitarium of heart disease.

William Graves Phillips, Maysville, Ky.; Jefferson Medical College of Philadelphia, 1909; member of the Kentucky State Medical Association; past president of the Mason County Medical Society; fellow of the American College of Surgeons; on the staff of the Hayswood Hospital; aged 52; died, July 5, in the Jewish Hospital, Cincinnati, of tumor of the brain.

Abram Whittemore Mitchell ✠ Epping, N. H.; University of the City of New York Medical Department, 1887; councilor of the Rockingham County Medical Society; past president of the New Hampshire Medical Society; at one time member of the state legislature; aged 73; died, July 31, in the Elliot Hospital, Manchester, following an operation for appendicitis.

Milo Melville MacKellar, Loveland, Okla.; College of Physicians and Surgeons, Keokuk, Iowa, 1896; past president of the Tillman County Medical Society; director of schools; on the staff of the Frederick (Okla.) Clinic Hospital; aged 61; died, August 18, in St. Mary's Hospital, Rochester, Minn., following an operation for glioblastoma multiforme.

Edwin Ellsworth Brophy, Meadville, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1907; member of the Medical Society of the State of Pennsylvania; served during the World War; formerly on the staff of the Meadville City Hospital; aged 62; died, July 26, of Parkinson's disease and coronary thrombosis.

Roy Fallas Mills ✠ Kansas City, Mo.; Rush Medical College, Chicago, 1912; associate in medicine, University of Kansas School of Medicine, Kansas City, Kan.; served during the World War; aged 55; on the staffs of the Kansas City General Hospital and the Bell Memorial Hospital, where he died, July 18, of endocarditis.

Frank Amos Crosby ✠ Lockport, N. Y.; Niagara University Medical Department, Buffalo, 1896; past president of the Medical Society of the County of Niagara; formerly member of the board of education; on the staff of the Lockport City Hospital; aged 63; died, July 13, of heart disease and nephritis.

Thomas Holmes Middlebro, Owen Sound, Ont., Canada; University of Toronto Faculty of Medicine, 1892; M. R. C. S., England, L. R. C. P., London, 1899 and F. R. C. S., England, 1900; fellow of the American College of Surgeons; on the staff of the Owen Sound General Hospital, aged 70; died, July 16.

John Mason Morris ✠ Louisville, Ky.; University of Louisville Medical Department, 1887; fellow of the American College of Physicians; aged 74; on the staffs of St. Anthony's Hospital and the Kentucky Baptist Hospital, where he died, July 21, as the result of injuries received in an automobile accident.

Baird Urquhart Brooks, Durham, N. C.; University of Maryland School of Medicine, Baltimore, 1905; member of the Medical Society of the State of North Carolina; served during the World War; aged 54; on the staffs of the Lincoln Hospital and the Watts Hospital, where he died, August 24.

John Walter McMahan ✠ Alma, Ga.; Tennessee Medical College, Knoxville, 1900; at one time member of the state legislature of Tennessee and state senator; health officer of Alma, and formerly health officer of Alcoa, Tenn.; aged 59; died, July 30, in a hospital at Waycross.

Herman Martinson ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1915; served during the World War; on the staff of the Sydenham Hospital; aged 44; died, August 19, in the Mount Sinai Hospital, of acute hepatitis and jejunal necrosis.

John Briggs Hagey, De Kalb, Ill.; University of Louisville (Ky.) Medical Department, 1902; member of the Illinois State Medical Society; past president and secretary of the De Kalb County Medical Society; city health officer; aged 65; died, July 29, of cerebral hemorrhage.

Louis Anthony Carlet, Washington, Pa.; Jefferson Medical College of Philadelphia, 1924; member of the Medical Society of the State of Pennsylvania; on the staff of the Washington Hospital; aged 35; died, July 14, in Philadelphia, of congenital polycystic kidney.

Henry B. Gaynor, Polk, Pa.; Temple University School of Medicine, Philadelphia, 1910; member of the American Psychiatric Association; clinical director of the Polk State Hospital; aged 65; died, July 21, in the Jeanes Hospital, Philadelphia, of malignancy of the bladder.

Roderick Frederick McHugh ✠ Aitken, Minn.; Milwaukee Medical College, 1912; formerly mayor of Aitken; on the staff of the Beecroft Hospital; served during the World War; aged 45; died, July 31, in St. Joseph's Hospital, Brainerd, of a gunshot wound of the chest.

Edward J. Dougher, Midland, Mich.; Baltimore University School of Medicine, 1898; member of the Michigan State Medical Society; secretary of the Midland County Medical Society; aged 71; died, July 26, in the Mercy Hospital, Bay City, of carcinoma of the colon.

William Harris, Mystic, Iowa; Milwaukee Medical College, 1912; member of the Iowa State Medical Society; served during the World War; on the staff of St. Joseph's Hospital, Centerville; aged 49; died, July 17, of heart disease and cerebral hemorrhage.

William Joseph Condon, New Brunswick, N. J.; Medico-Chirurgical College of Philadelphia, 1899; member of the Medical Society of New Jersey; served during the World War; aged 56; on the staff of St. Peter's Hospital, where he died, August 2.

Joseph Edward Windbiel ✠ Amsterdam, N. Y.; Albany (N. Y.) Medical College, 1908; served during the World War; on the staffs of St. Mary's Hospital and the City Hospital; aged 49; died suddenly, July 21, of acute dilatation of the heart.

Samuel Townsend Cousins, Wetumpka, Ala.; Birmingham Medical College, 1910; member of the Medical Association of the State of Alabama; aged 49; died, June 21, in St. Margaret's Hospital, Montgomery, of coronary occlusion.

Frank Herman Mohrman ✠ Cleveland; Cleveland College of Physicians and Surgeons, Medical Department Ohio Wesleyan University, 1910; on the staff of St. Luke's Hospital; aged 48; died, August 2, of coronary thrombosis.

George Norton Miller ✠ New York; Harvard University Medical School, Boston, 1882; aged 78; died, July 30, in the Vassar Brothers Hospital, Poughkeepsie, N. Y., of injuries received in an automobile accident.

Elihu P. Easley, New Albany, Ind.; University of Louisville (Ky.) Medical Department, 1872; member of the Indiana State Medical Association; formerly member of the city council; aged 87; died, August 2, of bronchitis.

William C. Griffin, Cartersville, Ga.; University of Nashville (Tenn.) Medical Department, 1878; member of the Medical Association of Georgia; aged 80; died, July 23, of chronic nephritis and uremia.

Benedict F. Shanahan ✠ Chicago; Bennett College of Eclectic Medicine and Surgery, Chicago, 1897; on the staff of the University Hospital; aged 63; died, August 2, in St. Luke's Hospital, of uremia.

Willis Le Baron Hale, North Attleboro, Mass.; Jefferson Medical College of Philadelphia, 1901; served during the World War; aged 58; died suddenly, August 11, of chronic myocarditis and nephritis.

Kenneth Marvin Adams, Gouverneur, N. Y.; Syracuse University College of Medicine, 1931; aged 30; on the staff of the Stephen B. Van Duzee Hospital, where he died, July 26, of pneumonia.

Cornelius B. Durham, Pineville, La.; Memphis (Tenn.) Hospital Medical College, 1912; member of the Louisiana State Medical Society; aged 49; died, June 30, in the Baptist Hospital, Alexandria.

Henry Laurence Shively, New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1888; aged 71; died, August 10, of cerebral hemorrhage.

Samuel Bernstein, Detroit; University of Oklahoma School of Medicine, Oklahoma City, 1916; aged 51; died, July 28, at Dunnville, Ont., of injuries received in an automobile accident.

Arthur Dunning Mansfield, Baltimore; University of Maryland School of Medicine, Baltimore, 1890; aged 67; died, July 27, of cerebral hemorrhage, arteriosclerosis and hypertension.

Samuel Ernest Parrott, Cordova, Tenn.; Memphis Hospital Medical College, 1901; aged 61; died, July 2, in the Methodist Hospital, Memphis, following an operation for appendicitis.

Henry Hiram Fuller, Hillsboro, Texas; (registered by Texas State Board of Medical Examiners under the Act of 1907); aged 68; died, July 25, of carcinoma of the face.

Adam Sharpe Gibson, Craik, Sask., Canada; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1912; aged 54; was killed, June 27, in an automobile accident.

William Holmes Ross ⊕ Patchogue, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1904; aged 54; died, September 3, of coronary thrombosis.

Arthur Ward Bowles, Detroit; University of Nebraska College of Medicine, Omaha, 1932; on the staffs of the Grace and Receiving hospitals; aged 26; was found dead, July 30.

John Warren Gard, Genoa, N. Y.; Albany (N. Y.) Medical College, 1914; health officer of the towns of Genoa, Scipio and Venice; aged 48; died, July 25, of acute myocarditis.

Edward Beach Loomis, Oak Park, Ill.; University of Vermont College of Medicine, Burlington, 1870; aged 87; died, July 28, of coronary thrombosis and arteriosclerosis.

Henry Hall Dodd, Millsboro, Del.; Baltimore University School of Medicine, 1897; served during the World War; aged 65; died, June 27, of carcinoma of the mouth.

Lester M. Brooks, Milwaukee; Milwaukee Medical College, 1912; member of the State Medical Society of Wisconsin; aged 46; died, July 23, of pulmonary tuberculosis.

William Daus, Cleveland; Western Reserve University Medical Department, Cleveland, 1884; aged 74; died, July 11, of cerebral hemorrhage and arteriosclerosis.

Frank Walton Larrabee, Boston; Dartmouth Medical School, Hanover, N. H., 1897; aged 65; died, August 8, of arteriosclerosis and cerebral hemorrhage.

Samuel Douglas, Indian Head, Sask., Canada; Victoria University Medical Department, Coburg, Ont., 1890; aged 75; died, in May, of abdominal hemorrhage.

Heaton Grant Daughters, Los Angeles; Kansas City (Mo.) Medical College, 1904; aged 68; died, July 16, of cerebral hemorrhage, nephritis and hypertension.

I. Clark Gary ⊕ Chicago; Chicago Medical College, 1889; aged 77; superintendent of the People's Hospital, where he died, July 4, of coronary thrombosis.

F. E. Shannon, Lebanon, Tenn. (licensed in Tennessee in 1889); member of the Tennessee Medical Association; aged 76; died, August 4, of uremia.

Joseph W. Propeck, Oak Park, Ill.; American Medical College, St. Louis, 1882; aged 76; died, July 15, of chronic myocarditis and nephritis.

Edward Cline Lidikay ⊕ Ladoga, Ind.; Medical College of Indiana, Indianapolis, 1903; aged 58; died, July 18, of carcinoma of the liver and rectum.

James Abston McFerrin, Mountpleasant, Tenn.; University of Nashville Medical Department, 1904; aged 55; died, July 21, of cerebral hemorrhage.

Joseph Raoul Richardson, Indianola, Miss.; Tulane University of Louisiana School of Medicine, New Orleans, 1924; aged 36; died, July 12.

P. B. Hall, Rush Springs, Okla. (licensed in Oklahoma under the Act of 1908); aged 76; died, July 15, in Marlow, of cerebral hemorrhage.

Nathaniel S. Macdonald, Sydney Mines, N. S., Canada; Dalhousie University Faculty of Medicine, Halifax, 1906; aged 58; died, May 22.

Frederick Hill Stanbro, Springville, N. Y.; University of Buffalo School of Medicine, 1887; aged 69; died, July 21, of cardiac infarction.

John Lewis Corum, West Chester, Ohio; Hospital College of Medicine, Louisville, Ky., 1904; aged 60; died, July 19, of heart disease.

James Joseph Morrow, Toronto, Ont., Canada; McGill University Faculty of Medicine, Montreal, Que., 1900; died, July 11.

D. Victor Desrosiers, La Sarre, Que., Canada; Laval University Faculty of Medicine, Quebec, 1902; aged 60; died in June.

John Curtis Pickett, Caledonia, Miss.; University of Nashville (Tenn.) Medical Department, 1905; aged 56; died, in July.

Rufus Choate, Washington, D. C.; Georgetown University School of Medicine, Washington, 1867; aged 88; died, July 26.

Leo Munter, San Francisco; Cooper Medical College, San Francisco, 1904; aged 60; died, July 1, of angina pectoris.

William Amos Dilts, Indianola, Iowa; College of Physicians and Surgeons, Keokuk, 1887; aged 75; died, July 8.

W. B. Leake, Jacksonville, Fla.; Atlanta Medical College, 1879; also a druggist; aged 78; died, June 1.

Philip W. Hawk, Zaleski, Ohio; Columbus Medical College, 1892; aged 72; died, July 5.

Correspondence

"REVERSED COLLES FRACTURE"

To the Editor:—In THE JOURNAL, June 29, page 2324, there appeared an article by Drs. Webb and Sheinfeld entitled "Reversed Colles Fracture, with Special Reference to Therapy," in which it was stated that no cases of successful reduction of this type of fracture by the closed method had been reported. I feel that I must take exception to this statement, since Dr. J. B. Roberts (Notes on the Modern Treatment of Fractures, New York, D. Appleton & Co., 1899, p. 134) showed the roentgenogram and reported such a case successfully treated by closed manipulation by his colleague Dr. M. J. Stern. Since the reason for the difficulty of closed reduction of this type of fracture is unexplained by the authors, it is of interest to recall the case presented before the New York Surgical Society by Dr. J. M. Hitzrot (*Ann. Surg.* **61**:740, 1915) in which attempted closed reduction was unsuccessful, operative intervention revealing that this was due to the piercing of the sharp distal end of the proximal fragment of the radius into the annular ligament. Reduction was easily performed after the proximal fragment was disengaged.

SIDNEY S. GAYNOR, M.D., New York.

[This letter was referred to George Webb of Brooklyn, who writes:]

To the Editor:—The case of a reversed Colles fracture successfully treated by closed manipulation by Dr. M. J. Stern was in a young boy. A prereduction roentgenogram showing the deformity is given in Dr. Roberts' book. However, there is no postreduction roentgenogram and the success of the reduction is merely gaged by the fact that the lad had "little or no" deformity after the reduction. This is not convincing evidence of a successful reduction, since it is well known that in early youth most deformities following fractures have a tendency to correct themselves. The fact that successful reductions of this type of fracture are made only in isolated cases seems to emphasize our statement that in the majority of cases satisfactory anatomic replacement of the distal fragment can rarely be accomplished other than by open operation.

SYMPATHECTOMY FOR THROMBO-ANGIITIS OBLITERANS

To the Editor:—In THE JOURNAL, June 29, was an editorial on "Sympathectomy for Thrombo-Angiitis Obliterans." This editorial is timely. About a year ago an editorial appeared in THE JOURNAL in which it was stated that sympathectomy had no place in the treatment of Buerger's disease. What I wish to call attention to, however, is the statement in the last paragraph: "It must be further emphasized that the operation (lumbar sympathectomy) is not only technically difficult even for the expert neurosurgeon but likewise a formidable procedure for the patient. The most serious complication is suppuration of the wound, which is particularly frequent in cases complicated by gangrene. The mortality even in the hands of the expert is not less than 4 per cent."

For years I have been advocating the use of the extraperitoneal approach to the lumbar sympathetics. Appearing in the July issue of the *American Journal of Surgery* was a description of this approach through a muscle-splitting incision. Perusal of this article will elicit the fact that I have performed in the neighborhood of 150 lumbar ganglionectomies, approximately thirty of which have been for Buerger's disease, and that the operative mortality is nil.

The operation performed in this manner is neither a tremendous operation for the surgeon nor is it a formidable one for the patient. Complications have been virtually absent.

The original retroperitoneal exposure was described by Royle. I have modified his operation several times until at last I have a muscle-splitting extraperitoneal approach in which it is possible to get the patient up on the third day and out of the hospital in less than a week. In other words, when there is need of operating on both sides it is still possible to do the operations either at one sitting or three or four days apart and still have much less hospitalization than is necessary in the transabdominal approach, not to mention the tremendously lessened mortality.

P. G. FLOTHOW, M.D., Seattle.

Queries and Minor Notes

ANONYMOUS COMMUNICATIONS and queries on postal cards will not be noticed. Every letter must contain the writer's name and address, but these will be omitted on request.

CALCIUM IN CHILD'S DIET

To the Editor:—It is my understanding that a quart of cow's milk contains approximately a gram of calcium and that this is considered the desirable amount for a growing child. Kindly answer or discuss the following questions: 1. How much calcium does a liter of human milk contain? 2. At different ages or different periods of growth do children require different amounts of calcium? Specify. 3. Is the ratio between calcium and phosphorus the same in cow's milk as in human milk? In the following questions it is understood that the hypothetic child is receiving an adequate supply of all the known vitamins and especially vitamin D. 4. If a healthy normally growing child between the ages of 2 and 14 years drinks a pint of milk each day and eats a good general diet containing liberal amounts of green vegetables and fresh fruits, is additional calcium indicated? 5. In the case of a healthy, normally growing child who drinks only a few ounces of milk each day or even none at all but who eats well of a normal and well balanced diet, should additional calcium be prescribed? 6. When additional calcium is necessary or desirable should it be administered in a form in which the calcium-phosphorus ratio is the same as in human milk? Name one or more such preparations and their relative merits. Is the calcium of some preparations more readily ionizable than that of others? 7. Discuss the merits or demerits of dicalcium phosphate, tricalcium phosphate, calcium lactate, calcium gluconate and calcium carbonate. 8. Is there any advantage in incorporating a calcium salt with cod liver oil? If so, which calcium salt should be preferred? In discussing the various calcium salts, please state the comparative costs of the various preparations, bearing in mind that a child with subnormal calcium intake in his diet might require medicinal calcium over a period of years. Please omit name.

M.D., Ohio.

ANSWER.—1. A liter of human milk contains about 1.24 Gm. of calcium.

2. The only way that this question can be answered is by a study of calcium and phosphorus metabolism experiments. Sherman has summarized the data from the literature and his table is here given.

Average Calcium and Phosphorus Storage of Children, in Grams per Kilogram Daily (Sherman and Hawley)

	Calcium				Phosphorus			
Age	No. of Cases	Intake	Output	Balance	No. of Cases	Intake	Output	Balance
1- 6 months	32	0.090	0.063	+0.027	11	0.075	0.058	+0.017
7-12 months	14	0.137	0.098	+0.039	5	0.115	0.087	+0.028
1- 2 years	5	0.089	0.070	+0.019	..	.....	.....	.....
3- 8 years	13	0.039	0.028	+0.011	10	0.054	0.046	+0.008
9-14 years	14	0.027	0.018	+0.009	11	0.039	0.029	+0.010

From a perusal of this table it is evident that the ratio of retained calcium to retained phosphorus alters with age. In the young child calcium is retained in excess while in older children phosphorus is retained in excess. From such a table it can be further stated that it is difficult to define calcium requirement without defining phoshorus requirement. A third variable is the exact amount of vitamin D in the diet.

3. The ratio of calcium to phosphorus in breast milk is about 2:2; in cow's milk, 1:3.

4. No, if his calcium metabolism is positive.

5. No, if his calcium metabolism is positive. It might be added, however, that absorption of calcium from milk is said to be greater than from other sources.

6. It has already been shown that as the child grows older the ratio of absorption varies and that therefore it would seem fair to say that the optimal calcium-phosphorus ratio would vary with age. The calcium of some preparations is more readily utilized than that of others.

7. From what has been said, the questioner should be able to draw his own conclusions as to the merits of the preparations mentioned. The various preparations are discussed in New and Nonofficial Remedies.

8. There is no advantage in incorporating a calcium salt with cod liver oil.

TREATMENT OF TUBERCULOSIS

To the Editor:—Dr. A states that he has treated over a thousand cases of pulmonary tuberculosis by means of rest in bed, general hygienic measures, ultraviolet rays to the chest twice a week, and injections of tuberculin subcutaneously twice a week. He reports uniformly good results and states that this treatment is rendered in all cases, irrespective of fever of 103 and 104 F. Dr. B holds that this treatment is not rational, as both tuberculin and ultraviolet rays are contraindicated in cases showing any marked elevation in temperature. Will you please give me the latest medical opinions regarding the use of tuberculin, particularly in the treatment of pulmonary tuberculosis? Please omit name.

M.D., Illinois.

ANSWER.—Dr. A does not state just what he means by uniformly good results; that is, whether all patients showed some evidence of improvement or all were restored to good working capacities. If nothing more was done for his patients than rest in bed, general hygienic measures, ultraviolet rays to the chest twice a week and injections of tuberculin subcutaneously twice a week, his treatment is approximately that of two decades ago and does not offer to his patients the advantages of the more valuable methods of treatment, such as collapse therapy. Moreover, Dr. A does not state the type of pulmonary tuberculosis or its extent. If he has treated more than 1,000 cases of frank pulmonary tuberculosis of the true clinical type and has restored all his patients to good working capacities, he probably holds the world's record for the treatment of tuberculosis. Moreover, if he has carefully selected 1,000 cases, many of only childhood tuberculosis or nonprogressive disease, it is still difficult to understand how every one of the entire 1,000 patients will continue on full working capacity long. Doubtless, Dr. B's criticism is on the ground that many of these patients should have had the advantage of other standard and more effective methods of treatment and that tuberculin and ultraviolet rays should be administered only in carefully selected cases.

While the pendulum swung far in favor of heliotherapy a few years ago, it has now settled back to approximately its proper place. It is not looked on as a panacea in the treatment of tuberculosis; it is only an adjunct and even in this capacity is administered only in carefully selected cases.

After Koch recommended tuberculin as a therapeutic measure, the pendulum swung far in its favor. Later when the good results anticipated were not forthcoming, the pendulum swung equally far in the opposite direction. At present there is a small group of physicians in this country who use tuberculin in the treatment of pulmonary tuberculosis. Nearly every one looks on it as a preparation to be avoided when any significant elevation of temperature is present. However, it is still considered helpful by a few workers in cases presenting but few or no symptoms, in which pulmonary lesions apparently have reached a standstill; that is, cases which are not definitely progressive or well under control. It is thought that in such cases tuberculin may result in a slight reaction around the lesion which simulates the hyperemia seen around a positive intracutaneous tuberculin reaction and that this may suffice to stimulate fibrosis. Most physicians believe that in any progressive pulmonary lesion tuberculin is not indicated.

The question arises as to whether the good results reported by some physicians following the administration of tuberculin as a therapeutic measure in carefully selected cases are not due to a partial and temporary desensitization. The fact is apparently well established that allergy to tuberculoprotein is responsible for the intense reaction about a focus of tubercle bacilli, which so frequently results in necrosis and cavitation. It is possible that tuberculin will be used much more extensively than at present, not to treat persons seriously ill with tuberculosis but to desensitize those who are highly allergic, in order to prevent intense reactions in case reinfection does occur. Partial desensitization has been found possible but, unfortunately, is only temporary. To insure against destruction, the tissues should be kept desensitized over a period of many years; that is, during those periods when tuberculosis approaches, reaches and descends from its mortality height. Obviously, this would be difficult to accomplish for many persons because of the long time necessary, as well as the expense. Tuberculin may still have an important part to play in tuberculosis, but at the present time this does not seem to be in the field of clinical, progressive disease with or without elevation of temperature.

AIR CONDITIONING NURSERIES

To the Editor:—Our hospital has recently been air conditioned and the question arose as to whether or not the babies should be taken out of the nursery to their mothers in the cool rooms. We have been raising the windows and wrapping the babies in light blankets and so far have had no trouble. Do you know of any instances in which a baby has contracted a cold under these circumstances?

EDWIN C. MCMULLEN, M.D., Pine Bluff, Ark.

To the Editor:—I shall greatly appreciate a letter from you, stating your opinion of the advantages of air conditioned infant nurseries over nurseries that are not air conditioned, for both summer and winter months. We are located fairly well south but have extreme temperatures around 106 F. in summer and some subzero in winter.

K. C. REESE, M.D., Tulsa, Okla.

ANSWER.—Only a few hospitals have been air conditioned; consequently data are not available on which to base a reply. But if a common sense view of the situation is taken, it would not seem a hazard to take a normal nursing infant from the nursery to an air cooled room. The moment the baby leaves the nursery and is taken into the hall, he experiences at once a change of temperature. In the cooler season of the year, particularly in the winter, the baby is taken outdoors, where he is subjected to a decided change in temperature, which may amount to from 35 to 50 degrees F. or more. Ordinarily the babies suffer no unfavorable consequences from being taken outdoors in the winter, particularly if they are properly clad and extreme chilling and high winds are avoided.

The answer to the question would seem to be that a baby may be carried into an air cooled hospital room if he is sufficiently protected by proper clothing or a blanket.

There can be little doubt that high temperatures of summer, reaching an extreme of 106 and heated hospitals in subzero weather are not conducive to the best of health, for either infants or adults. When the cold air of winter is heated in a building, it expands and becomes dry unless some device is provided to humidify it. It often requires a temperature of 80 F. or more for heated dry air to be comfortable. During and following heat waves of summer, even with a maximum temperature of no more than 100, a good many deaths are reported among elderly and somewhat debilitated persons as being directly due to the heat. Doubtless, many others die from conditions that might be indirectly accounted for by high temperature. It would seem more than likely that there is considerable loss of life in infancy, either directly or indirectly, from the high atmospheric temperature.

The Chicago Ventilation Commission (Report of Chicago Commission on Ventilation, 1914) and the New York Ventilation Commission (Ventilation Report of the New York State Commission on Ventilation, New York, E. P. Dutton & Co., 1923) found that three physical qualities, namely, temperature, humidity and circulation of air, are important not only for comfort but also for the health of human beings. The temperature found best was approximately 68-70 F., with a relative humidity of from 40 to 50 per cent, with the air slowly circulating.

Blackfan and Yaglou (*Am. J. Dis. Child.* **46**:1175 [Nov., part 2] 1933) made a careful study of atmospheric conditions on the growth and development of premature infants, using as controls normal, full-term infants. These workers had available unconditioned as well as conditioned nurseries, so that they could make comparisons of results in the two types. They found that in premature infants the heat-regulatory mechanism was not adequate to protect them against either too high or too low temperatures. A humidity of 65 per cent, with a temperature ranging from 75 to 100 F., was found best. Of course, each premature infant had to be treated individually because of differences in body weight, fetal age, and so on. A humidity as low as 30 per cent often led to serious consequences. The net mortality for all weight and age groups was 28.9 per cent in the unconditioned nursery as compared with 7 per cent in the conditioned nursery. Infections both acute and chronic accounted for 70.3 per cent of the total number of deaths in the unconditioned nursery and 31.9 per cent in the conditioned nursery. They state that in the light of their study the importance of optimal temperature, humidity and ventilation conditions in the growth and development of premature infants is demonstrable.

Obviously the special air conditioning employed by Dr. Dafoe may have been helpful in saving the lives of the quintuplets. As the heat-regulatory mechanism is adequate to protect normal, full-term infants, they do not require the high degree of temperature or the high relative humidity that premature infants need. Therefore, in nurseries for such children ordinary air conditioning suffices. There is no question about the advantage of conditioning the air so that the temperature is held constantly at that degree which has been found best for the body and with a relative humidity in which the body thrives best with a slow circulation of air and all dust and other contamination filtered from it.

SLIGHT FEVER DURING PREGNANCY

To the Editor:—A woman, aged 26, is pregnant the second time. With both pregnancies her temperature has been as high as 99.6 F. Apparently the elevation of temperature begins about six weeks after the onset of pregnancy. With the first pregnancy the fever stopped at about the sixth month. She is now in the third month of the second pregnancy and has a fever. At the first delivery, which was a very difficult one, I noted that the patient was almost without amniotic fluid. I was wondering whether the fever absorbed this fluid. The patient is a nurse and went through training without missing a single day. Her weight before marriage was 120 pounds (54 Kg.). It increased with the first pregnancy to 150 pounds (68 Kg.). From the genito-urinary standpoint she is normal. Nothing can be found to account for any elevation of temperature. The ears, nose, eyes and throat are normal, with the exception of the small deflected septum. The specialist says that this is not causing the fever. The tonsils have been removed. The teeth are in good condition. The patient began menstruation at the age of 14 years. Menstruation lasted for seven days up until the age of 18 years, when dysmenorrhea developed, after which the duration gradually declined to about four or five days. She was married at the age of 24, after which menstruation was cut down to about three days, which continued as such until three months before pregnancy and then became a day and a half. While in training the hemoglobin was from 80 to 85. At present it is between 70 and 80. With this temperature she does not have any night sweats. The physical examination of the chest apparently gives normal results. I have never roentgenographed the chest. When the patient is not pregnant she has a normal temperature. The urine has always been normal. The blood pressure is around 100, being a little low. The action of the bowels is satisfactory with an occasional dose of magnesia magma. She is said to have had an attack of appendicitis at the age of 15 but has had no further trouble. There have been no abdominal operations. She was told that she had a cardiac leakage but I cannot make out anything wrong with the heart. During her pregnancies I have kept her on a well balanced diet with a quart of milk a day. The patient presents a rather normal history all the way through but I am wondering if she has a mild toxemia of pregnancy which is manifesting itself through this slight elevation of temperature. She has an occasional headache. A Wassermann test was not made. I do not believe that chronic malaria would manifest itself as such in this way. The patient was born in the malarial belt. There is no tuberculous history in the family as far as she can recall. Please omit name.

M.D., Florida.

ANSWER.—A slight degree of fever during pregnancy may be found in not a few cases in prenatal clinics and it is rare that any pathologic change is discoverable to account for it. Older writers mentioned a "fever of pregnancy" but modern investigations have shown that tuberculosis, pyelitis, appendicitis, allergy and other causes were operative. If the patient is well there is no reason for any concern on the part of the physician.

SYPHILITIC MENINGO-ARTERITIS

To the Editor:—A man, aged 30, had a sore on the penis five years ago. Six weeks ago he had a sudden attack of severe headache and partial paralysis of the left arm. Today he is weak, very nervous, has a shaking of the left leg, controlled by placing his foot on the floor, and he can move the left arm fairly well. He had a positive Wassermann reaction, and spinal puncture controlled the headache. Is it possible for syphilis to cause such an attack of the brain and cord system five years after the primary lesion? Would regular antisyphilitic treatment suffice? Please omit my name if printed.

M.D., Minnesota.

ANSWER.—The patient is undoubtedly suffering from a syphilitic meningo-arteritis, probably of a localized type and with sufficient extension to have caused pressure on important nerve paths following a localized hemorrhage. It of course is difficult to place this focus, but it probably is above the decussation on the right side.

It is unfortunate that the correspondent did not mention the condition of the spinal fluid. Undoubtedly the patient has a high cell count, a positive globulin, an increase in the central zone of the colloidal gold curve, and a positive Wassermann reaction on the spinal fluid. He should be put on antisyphilitic treatment at once. Potassium iodide in 0.5 Gm. doses should be given after meals, and for two weeks the intramuscular injection of the aqueous solution of sodium bismuth tartrate, 0.2 Gm., or of iodobismitol, 2 cc., or of sodium bismuth thioglycollate, 0.2 Gm., every other day. The patient might then be started cautiously on neoarsphenamine injections intravenously, the first dose being 0.3 Gm., followed in five days with a dose of 0.6 Gm., and if the patient stands this all right, an injection of 0.75 Gm. every week until he has received a total of twelve injections of the arsenical. Following the last injection of the arsenical, the patient may be given an injection of one of the bismuth suspension preparations, for example, bismuth salicylate or potassium bismuth tartrate, these injections

being given once a week for a series of ten injections, to be followed with twelve further injections each of 0.75 Gm. of neoarsphenamine, this in turn to be followed by a further course of bismuth injections. If the patient stands this therapy well he should have three or four courses of the arsenical and of the bismuth preparation. A Wassermann test should be taken at the end of each course of treatment and a lumbar puncture every six months to observe progress. Certain cases of this type respond nicely to antisyphilitic therapy, though it is well to get the therapy started before the hemorrhage has had an opportunity to become too firmly organized, and in an important condition of this type, if there is any question as to the method of handling the patient, one should have the patient consult a well trained syphilologist. It may mean the difference between a permanent disability and complete recovery.

DOSAGE OF ROENTGEN RAYS

To the Editor:—Please give me the number of roentgens required to give an erythema dose on a skin area of 10 by 10 cm. with the following settings:

100 kv., 5 ma., no filter.
100 kv., 5 ma., 1 mm. of aluminum.
125 kv., 5 ma., no filter.
125 kv., 5 ma., 1 mm. of aluminum.
125 kv., 5 ma., 3 mm. of aluminum.
160 kv., 5 ma., 0.25 mm. of copper plus 1 mm. of aluminum.
175 kv., 5 ma., 0.25 mm. of copper plus 1 mm. of aluminum.
200 kv., 5 ma., 1 mm. of copper plus 1 mm. of aluminum.
200 kv., 5 ma., 0.5 mm. of copper plus 1 mm. of aluminum.
200 kv., 5 ma., 0.75 mm. of copper plus 1 mm. of aluminum.

At 100 kilovolts without filtration the skin will generally tolerate 350 roentgens with a hardly noticeable erythema on the tenth day. Recently I have seen recommended 900 roentgens as an erythmea dose when 200 kilovolts is used filtered through 1 mm. of copper plus 1 mm. of aluminum. This seems to me to be too much. I shall appreciate a statement from you as to what is considered an average erythema dose with the foregoing factors.

G. E. HENSCHEN, M.D., Sherman, Texas.

ANSWER.—Under exactly similar physical conditions the output of different generators of x-rays, measured in international roentgens, should be the same. In ordinary practice, however, exactitude of physical conditions seldom obtains. Moreover, erythema represents a biologic reaction of the skin, and the tolerance of different skins varies considerably. For these reasons the dose in roentgens required to induce erythema depends on the generating apparatus and tubes, the conditions under which these are operated, the conditions of measurement, the tolerance of the subject's skin, and the degree of erythema taken to represent the erythema dose. Measurement of the x-ray output of different installations may vary within fairly wide limits. Also, measurement with an ionization chamber in air or with the chamber in contact with the skin gives widely different results. In the latter case the scattered radiation is included, whereas in the former it is excluded.

In all probability the erythema dose of 900 roentgens mentioned by the enquirer represented a dose measured with the ionization chamber in contact with the skin, which would roughly be about 40 per cent greater than the number of roentgens registered by the ionization chamber if the measurement had been made with the chamber free in air. Measured in air, the average erythema dose, with a peak voltage of 140 and with filtration of 6 mm. of aluminum, should be from 550 to 600 roentgens. With higher voltages and greater filtration, a somewhat larger dose may safely be given.

MALIGNANT GROWTHS OF ANTRUM

To the Editor:—How frequently do malignant growths of the maxillary antrums occur, as determined clinically and radiographically? References on epiphyseal development in standard anatomy textbooks do not coincide in all age periods as checked by roentgen examination. Have any comprehensive roentgen studies been made recently? Please omit name.

M.D., New York.

ANSWER.—Malignant growths of the antrum are relatively infrequent. The number of this type of new growth as compared with the total number of patients frequenting several of the world's largest nose and throat clinics gives figures varying from 0.03 to 0.12 per cent.

Another source states that malignant neoplasms of the nose and its accessory cavities represent about 1 per cent of all malignant growths and about 1 in 800 of all cases of nasal disease.

A search of the literature does not reveal any roentgen studies of the maxillary sinus devoted solely to the discovery by this method of the incidence of carcinoma in this region.

Perhaps, one answer to the question would be the statement of one authority (Oehngren), who feels that "a more widespread use of x-rays for diagnosis in the case of pains in the trigeminal nerve area and a more general use of them in unilateral subacute rhinitis in those over the age of 50 would result in a smaller number of overlooked tumors of the antrum. Too many of them in the past have been going about for months with a diagnosis of neuralgia or toothache."

There is no exact agreement on the question of epiphyseal development because of normal variations. In general, the anatomists agree and their observations coincide more or less with those of the roentgenologists (Cohn, Isadore: Normal Bones and Joints, New York, Paul B. Hoeber, Inc., 1924).

CONJUNCTIVAL IDIOSYNCRASY TOWARD ARSENIC AND BISMUTH

To the Editor:—I am treating a messenger boy weighing about 121 pounds (55 Kg.) for syphilis. I began by giving him 0.45 Gm. of neoarsphenamine every five days for six injections and then every seven days for another six injections. I followed with 0.2 Gm. of sodium bismuth thioglycollate intramuscularly every seven days for twelve doses. Then I omitted treatment for three weeks and drew blood for a Wassermann test, which was negative. I then began again on the same routine as before. The boy rode a bicycle every day except Sundays all through the winter. He is in excellent physical and mental condition and cooperates intelligently in every way. On the day after the first neoarsphenamine injection a slight conjunctivitis developed in both eyes, with a marked increase in the flow of tears. The conjunctivitis subsided when the eyes were protected by goggles when he was in the open air but the flow of tears is so intense that often he will have patches of moisture covering nearly the entire front of his coat. There seemed to be no difference when he was treated with arsenic and bismuth compounds. After his three weeks' rest period he was almost back to normal, when on the day after the first injection of the second course the process appeared as violent as before, or perhaps more so. I have never had this complication confront me before, although I have treated many such patients in much the same way. What I wish to know is whether or not there is any possibility of real danger to the eyes, and how to treat the condition so that he can keep at his job in the open air. Please omit name and address.

M.D., Illinois.

ANSWER.—Without specific knowledge as to the appearance of the conjunctiva and cornea, it is rather difficult to answer the question. Apparently there does not seem to be any interstitial keratitis present, but merely an epiphora consequent to the administration of arsenic or bismuth compounds. As there are remissions of the lacrimation in the rest periods, it is evident that dacryocystitis is not present. Consequently, this must be one of those extremely rare cases of a conjunctival idiosyncrasy toward arsenicals or bismuth. Reference to this can be found in the Kurzes Handbuch der Ophthalmologie, volume 7, Syphilis and the Eye, by Igersheimer, page 173, wherein cases reported by Simon, Naegeli, Kleeberg and Kraus are cited. The only relief that can be obtained is to treat the syphilitic condition with mercury and iodides instead of arsenic or bismuth compounds.

DISCOLORATION OF HAIR AFTER PERMANENT WAVE

To the Editor:—An unmarried woman, aged 43, complains of a yellowish color beginning at the scalp line extending out on the shafts of the hair following permanent waves. She has been bothered with this condition for six years ever since receiving her first wave. The hair is healthy, it is prematurely grayed, and there are no scalp disturbances. Six years ago a total thyroidectomy was performed, two years ago a suprapubic hysterectomy, and some years ago a tonsillectomy. Physical examination and a complete laboratory check-up are all negative. She further states that four years ago she reported to some physician who administered heavy doses of alkali, which seemed to give relief for a while. The only other significant fact in the history is constipation, which is not very marked. Examinations of the urine and the blood are all negative. The Wassermann reaction is negative. Can you give me some idea as to why this peculiar yellow pigment seems to be depositing in the hair shafts? I will appreciate any suggestions as to treatment.

M.D., New York.

ANSWER.—Yellow hair is not uncommon in cases of icterus and has occurred after the use of resorcin lotions. No report of yellow hair after the permanent wave procedure has been found, but Philipsen (Green Discoloration of the Hair After Permanent Waving, *Ugesk. f. Læger* **95**:746 [June 29] 1933) reports green hair in seven of his patients after the permanent wave. All had previously used lotions containing mercury solutions. He remarks that it is no wonder that a mercurial solution in combination with an alkali under great heat should undergo a chemical reaction. So far as his experiments had been carried, he had found no other chemical that reacted under these conditions. The sulphur in the hair is, he thinks, in too firm a combination to cause any change of color.

In the case described, the color is confined to the portion of the hair shaft next the scalp. This would suggest that the color was due to something on the scalp. Is the patient taking

iodine or bromine? The ammonia salts of these halogens turn yellow on exposure to the air. Has resorcin or naphthol been used on the scalp?

Unless some such cause can be found and removed, treatment must be limited to the substitution of milder methods of hair curling for the popular permanent wave.

ANTIMENINGOCOCCUS SERUM

To the Editor:—I should like to know whether there is any value in a prophylactic injection of antimeningococcus serum given hypodermically on the day of exposure. Is any immunity conferred by such use of a serum supposedly adapted for intraspinal injection? Would intramuscular injection cause less reaction (anaphylactic) or more than hypodermic? Three years ago one brand was given hypodermically to two patients without any other ill effects than a sore arm temporarily. Recently, of three patients who received a different brand, two suffered a severe urticaria a week after the injection, while the other patient suffered a pyrexia of 101 F. beginning two days after the injection and lasting ten days; the latter's arm was very red and inflamed, while the arms of the patients with urticaria suffered little pain at the site of injection. If the serum has a prophylactic value, what amount should be given? Please omit name.

M.D., California.

ANSWER.—There is ground for belief that antimeningococcus serum has prophylactic virtues. Ordinarily the preventive effect would last only three or four weeks. Practically the same preventive effect, or passive immunity, would result from intramuscular as from intraspinal injection. The danger of serum reaction would be about the same, no matter what the route of injection. Serum reactions depend on the sensitivity of the patient, the brand of serum and the age of the serum. Different brands of serum vary in their content of reaction-producing substance, and older serums are regarded as less dangerous than recent. No effective dose has been established for preventive purposes; it would seem reasonable to give at least a full therapeutic dose. The fact that such preventive injection may sensitize the subject to horse serum should be borne in mind.

UNDULANT FEVER AND PREGNANCY

To the Editor:—I have a patient, four and a half months pregnant, who has undulant fever. From her history I judge that she apparently has had the infection about twelve months. Should the infection fail to subside before her delivery, is it most likely that the new-born infant will be similarly infected? If so, what line of treatment is recommended? At present the patient is being treated with Brucella melitensis vaccine (Lederle), tonics and general hygienic care. Any information relative to the handling of this case would be appreciated. The patient's general physical condition is not bad. She was not aware that she had any fever at any time until demonstrated by a thermometer. There is a small dental root abscess, as shown by the x-rays. She has a slight anemia (erythrocytes 3,700,000, hemoglobin 65 per cent). The urine, Wassermann and Kahn reactions, blood urea and basal metabolic rate are all normal. The temperature fluctuates between 97 and 100 F. and the pulse between 78 and 94 at complete rest in bed and 88 and 120 when up and about. The agglutination test is positive for undulant fever.

M.D., Arkansas.

ANSWER.—It is quite unlikely that the child will exhibit evidence of undulant fever. This statement is based on the fact that calves born of cows with brucellosis rarely, if ever, show evidence of the disease.

AMINOACETIC ACID IN MYASTHENIA

To the Editor:—I saw a case of pseudohypertrophic muscular dystrophy or myopathy in a child, aged 7 years. Is there anything new in the treatment for such cases? Would the induction of artificial hyperpyrexia be of any benefit in a case of this kind? Is there any hospital or clinic to which I could send this child for further study?

J. L. SNAVELY, M.D., Sterling, Ill.

ANSWER.—The administration of aminoacetic acid has been advocated in the treatment of myasthenia and myopathy, though the value and limits of its usefulness have not been determined. Many neurologists and most neurologic departments of university medical schools are interested in this problem.

GANGRENE OF UTERUS

To the Editor:—At autopsy a uterus is found black and gangrenous. How long would this condition take to develop? (The case in question is a possible criminal abortion at approximately three months and I can find nothing in my reference books regarding it.) Kindly omit name.

M.D., California.

ANSWER.—It is not possible to answer this question satisfactorily without further information. All that can be said is that discoloration and gangrenous changes may develop in the course of a day or so after abortion.

Medical Examinations and Licensure

COMING EXAMINATIONS

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Written examination and review of case histories of Group B applicants will be held in various cities of the United States and Canada, Dec. 7. *Applications must be filed not later than Nov. 1.* Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: St. Louis, Nov. 18. Sec., Dr. William H. Wilder, 122 S. Michigan Ave., Chicago.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: St. Louis, Jan. Sec., Dr. Fremont A. Chandler, 180 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PEDIATRICS: Philadelphia, Oct. 10 and St. Louis, Nov. 20. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF RADIOLOGY: Detroit, Dec. 1-2. Sec., Dr. Byrl R. Kirklin, Mayo Clinic, Rochester, Minn.

ARIZONA: Phoenix, Oct. 1-2. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: *Basic Science.* Little Rock, Nov. 4. Sec., Mr. Louis E. Gebauer, 701 Main St., Little Rock.

CALIFORNIA: Sacramento, Oct. 21-24. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

COLORADO: Denver, Oct. 1. Sec., Dr. Harvey W. Snyder, 422 State Office Bldg., Denver.

CONNECTICUT: *Basic Science.* New Haven, Oct. 12. *Prerequisite to license examination.* Address, State Board of Healing Arts, 1895 Yale Station, New Haven.

GEORGIA: Atlanta, Oct. 8-9. Joint-Secretary, State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

IDAHO: Boise, Oct. 1. Commissioner of Law Enforcement, Hon. Emmitt Pfost, 205 State House, Boise.

ILLINOIS: Chicago, Oct. 22-24. Act. Supt. of Regis., Dept. of Regis. and Edu., Mr. Clinton P. Bliss, Springfield.

MICHIGAN: Lansing, Oct. 8. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 202-3-4 Hollister Bldg., Lansing.

MINNESOTA: *Basic Science.* Minneapolis, Oct. 1-2. Sec., Dr. J. C. McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical.* Minneapolis, Oct. 15-17. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MONTANA: Helena, Oct. 1. Sec., Dr. S. A. Cooney, 7 W. 6th Ave., Helena.

NEBRASKA: *Basic Science.* Lincoln, Oct. 1-2. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: Carson City, Nov. 4. Sec., Dr. Edward E. Hamer, Carson City.

NEW JERSEY: Trenton, Oct. 15-16. Sec., Dr. Arthur W. Belting, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, Oct. 14. Sec., Dr. Le Grand Ward, Sena Plaza, Santa Fe.

RHODE ISLAND: Providence, Oct. 3-4. Dir., Department of Public Health, Dr. Edward A. McLaughlin, 319 State Office Bldg., Providence.

WEST VIRGINIA: Huntington, Oct. 28. State Health Commissioner, Dr. Arthur E. McClue, Charleston.

WYOMING: Cheyenne, Oct. 7. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

Minnesota June Examination

Dr. Julian F. Du Bois, secretary, Minnesota State Board of Medical Examiners, reports the oral, written and practical examination held in Minneapolis, June 18-20, 1935. The examination covered 12 subjects and included 60 written questions. An average of 75 per cent was required to pass. Forty candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Colorado School of Medicine		(1933)	90.1
Yale University School of Medicine		(1932)	85.4
Loyola University School of Medicine		(1934)	91.3
Rush Medical College	(1934) 91.2,	(1935)	84.1
Johns Hopkins University School of Medicine		(1933)	89.2
University of Minnesota Medical School	(1933) 91.3, (1934) 80.3,* 84.2,* 86,* 86.1,* 87.3,* 89.1, 90,* 90.4,* 90.5,* 91.6,* 94.2,* (1935) 84,* 85.1, 87.1,* 88, 88.5,* 89,* 89.3, 89.3, 90,* 90.1,* 90.2,* 91.2,* 91.5,* 92.1*	(1930)	87.1,
Creighton University School of Medicine		(1935)	90.2
Duke University School of Medicine		(1932)	89
University of Virginia Department of Medicine		(1930)	89.6
Marquette University School of Medicine		(1935)	89.2, 89.4, 90.2
Rijks-Universiteit te Leiden Faculteit der Geneeskunde, Netherlands		(1928)	87.5

* This applicant has received an M.B. degree and will receive an M.D. degree on completion of internship.

California Reciprocity and Endorsement Report

Dr. Charles B. Pinkham, secretary, Board of Medical Examiners of the State of California, reports 18 physicians licensed by reciprocity and 3 physicians licensed by endorsement from June 20 through Aug. 1, 1935. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Colorado School of Medicine		(1933)	Colorado
Hering Medical College, Chicago		(1897)	Illinois
Northwestern University Medical School		(1924)	Iowa, Colorado
Rush Medical College		(1932)	Illinois
State University of Iowa College of Medicine		(1927)	Washington

Kansas City Hahnemann Medical College, Missouri	(1909)	Kansas
Washington University School of Medicine	(1924)	Kansas
Creighton University School of Medicine	(1933)	Nebraska
John A. Creighton Medical College	(1917)	Nebraska
University of Nebraska College of Medicine	(1925), (1934)	Nebraska
Columbia Univ. College of Physicians and Surgeons	(1916)	New York
Cornell University Medical College	(1932)	New York
Willamette University Medical Department, Oregon	(1907)	Oregon
Temple University School of Medicine	(1932)	Penna.
Vanderbilt University School of Medicine	(1931)	Mississippi
Universität Heidelberg Medizinische Fakultät	(1930)	Minnesota

LICENSED BY ENDORSEMENT

School	Year Grad.	Endorsement of
Harvard University Medical School	(1930)	N. B. M. Ex.
Marquette University School of Medicine	(1934)	N. B. M. Ex.
University of Toronto Faculty of Medicine	(1929)	N. B. M. Ex.

Book Notices

Backache. By James Mennell, M.A., M.D., B.C., Medical Officer, Physico-Therapeutic Department, St. Thomas's Hospital. Second edition. Cloth. Price, $3.50. Pp. 227, with 59 illustrations. Philadelphia: P. Blakiston's Son & Co., Inc., 1935.

In this edition the author has added more than thirty pages and eleven illustrations. The book is ingeniously illustrated in red and blue, the former showing the patient and the latter the examiner or manipulator, presenting instructive outlines. The differential diagnosis and treatment of the various causes of backache have advanced remarkably. The book represents the work of eleven years, including his study during two visits to the United States. The author states that he has presented nothing that lies outside his personal experience. He deals with the simplest technic. He has been conservative and described only the more simple of the manipulations that can be put to daily use. He calls attention to the inadequacy of the routine examination of the back as generally practiced and the injustice of the opinion formed in the early period of his study of backache that all the patients grossly exaggerated the symptoms and that the symptoms themselves were to a considerable degree neurasthenic, often almost amounting to delusion. The author believes that it is only as a result of an adequate routine examination that one can arrive at a definite diagnosis. He has elaborated a complete method of examination. He believes that most of the pitfalls in the diagnosis of backache can be overcome or evaded by careful history taking. The book is to be highly recommended.

Entstehung und Funktion von Gefässystem und Blut auf cellular-physiologischer Grundlage. Von Dr. med. Max Hausmann. Paper. Price, 56 Swiss francs; 44.80 marks. Pp. 704, with 207 illustrations. Basel: Verlag Benno Schwabe & Co., 1935.

This volume is of especial interest to the student of zoology, anatomy and physiology. The author is a Swiss physician who in thirteen years of assiduous labor has found the time and energy for this extensive work. On the whole, the book represents an attempt to combine the views, theories and results of specialized research in the fields of zoology, embryology, physiology, hematology, pathology and clinical medicine. The author justly points out that intensive specialization has led too often to incomplete solutions of general biologic problems. The volume is essentially theoretical and contains no experimentally gained contributions by the author.

The vast literature pertaining to this field is critically reviewed. Throughout the book it is evident, however, that American literature has hardly been consulted by the author, a tendency that is all too common with European writers.

To the clinician the book will be of interest particularly in its chapters dealing with the reticulo-endothelial system, the origin of red blood corpuscles and of leukocytes, the hematopoietic organs, the physiology of capillaries and the physiology of the circulatory system as a whole.

The theoretical views of the author are expressed in the introductory chapter and are summarized in the final chapter. The body of the book represents mainly documentation for his deductively gained opinions and consists of three parts, each containing reviews of pertinent phylogenic and ontogenic studies and theories of the circulatory system (part I, invertebrates, pp. 10-216; part II, vertebrates [early stages] pp. 217-400; part III, vertebrates [later stages] and physiologic synthesis, pp. 401-634).

The author's discussion of the morphogenesis of the vascular system is based on Arnold Lang's theory of the trophocoele. A summary of this theory and detailed discussion is given in chapters 2 and 3. Hausmann accepts Lang's views as a profitable and stimulating hypothesis although he recognized certain objections and finds it necessary to apply it less vigorously than its founder. Indeed, the author emphasizes that it is impossible to explain the origin of the vascular system by a general morphologic theory applicable to all classes of the animal kingdom.

The question of the origin of endothelium is recognized as a particularly difficult problem. With respect to endothelium in vertebrates, the author refers to the views of Fernandez and Näf, former pupils of Lang, who accept its mesenchymal origins. Hausmann is disinclined to believe, however, that this is true for all metazoa. Important American contributions to this problem by Evans, Hockard and Reagan are not discussed. The work of Evans is merely referred to, indirectly from Keibel and Mall's handbook. With regard to the local origin of endothelium, the author's discussion is centered on Hatta's work.

That the author is strongly influenced by Lang's theory, in spite of its admitted limitations, is evident by the fact that he sees no difficulty in considering the vascular endothelium of vertebrates as derived from separated coelomic elements. The endothelial linings would thus represent a secondary coelomic cavity. Similarly, Hausmann considers the blood islands of the yolk sac as emigrated coelomic elements which secondarily produce the capillary network. The theory of His of the parablast is considered antiquated and has been abandoned.

In the introductory chapter the author states that a true lymphatic system with endothelial linings of its channels appears for the first time in birds. This statement reveals that the author has not looked deeply and widely into the literature pertaining to that system, for the unquestioned existence of such a system in the vertebrates below the birds—in fishes, amphibia and reptiles—has been accepted for a century. He accepts without discussion the direct origin of lymphatics by outgrowth from veins, a statement which shows again that he has not taken the trouble to acquire thorough information about established investigations in this matter (Huntington, McClure, Kampmeier).

The book contains no independent chapter on the lymphatic system; there are, however, subtitles dealing with lymphoid organs and lymphatics in chapters 23, 26 and 27. Although the author points out, in these summary discussions, the preeminence of American anatomists in this field, the only author indirectly quoted is Sabin, whose views he accepted without question. Hausmann passes over in silence the evidence contained in a great number of researches on the origin and development of the lymphatic system which refute the views of Sabin.

The author's main thesis centers in the consideration of the function of an organ or organ system not as a narrowly circumscribed partial function of the organism as a whole. Hausmann perceives an organ and, indeed, the entire organism as the result of a synthesis of cells which carry all primary functional characteristics and which gain their specific function only through influences of their particular environment. His views represent a closer correlation of phylogenic and ontogenic origin with principles of general physiology of the cell. The analysis of the vascular system from this point of view was undertaken as an example and test for the validity of such an approach.

It may be questioned, however, whether the author has been successful in escaping the dangers that are innate in any such attempt to fit biologic facts and theories with deductively preconceived opinions. Modern biology is not being written in a study or in libraries. The author exhibits a tendency toward verbosity that does not add to the clearness of his argument.

The book is excellently printed. The illustrations are borrowed from original papers and credit is given to the respective sources. Fifteen diagrams are the author's own. A valuable feature of the large volume consists in marginal titles on every page. There is an excellent subject and author's index. The subject index gives helpful definitions for many zoological, anatomic and physiologic terms.

The Doctor's Bill. By Hugh Cabot. With an introduction by A. Lawrence Lowell. Cloth. Price, $3. Pp. 313. New York: Columbia University Press, 1935.

The first three chapters survey general medical developments and resources in this country. They contain a description of the complexity in medical practice due to the development of hospitals and specialization. A chapter on the general practice of medicine conveys the idea that the general practitioner is being crowded out of the field, a conclusion that is emphasized in the next chapter, on specialists and group medicine. In this the author argues the superiority economically and medically of group practice. This argument is continued in the succeeding chapters, in which he accepts without question the conclusions of the Committee on the Costs of Medical Care as to lower costs of group practice and endorses the practice of contract medicine by groups.

The author recognizes the abuses that have grown up under workmen's compensation but does not seem to recognize that these abuses are closely connected with some of the forms of contract practice associated with compensation administration.

There is a review of health insurance in continental Europe and the British Isles, in which these systems are presented from a much more favorable point of view than a wider knowledge of those systems would seem to justify. Nevertheless, the author concludes, "I cannot convince myself that the conditions in this country can be satisfactorily met by transplanting plans which are, at least apparently, satisfactory in other countries." He also says: "Some study of the problems in Europe leads me to the opinion that a grade of medical service which is apparently entirely satisfactory, and probably fairly meets the demand in various of those countries, would fall short of the demand here, and would prove unsatisfactory." He is under the impression that "the subdivision of the field of medicine and the development of specialization have on the whole gone considerably further in this country than abroad." This conclusion is not in accord with facts.

The author's discussion of medical needs in the United States again follows the conclusions of the Committee on the Costs of Medical Care and among "suggested methods of improvement" are various systems of voluntary insurance, especially medical insurance by private groups of physicians. In regard to the recent movement of county medical societies to organize medical service he says: "If the medical profession can succeed in delivering a satisfactory article of medical service through the united efforts of organizations such as the county medical societies, it will have gone far to justify its claim of being capable to handle such problems on its own initiative." He enters into some controversial questions within the American Medical Association and accepts the purported statements of some of the critics of the American Medical Association but shows that he is thoroughly unfamiliar with many of the facts.

In his final chapter, "Where Do We Go from Here?" he criticizes the demand of the medical profession for free choice of physician and urges an expansion of public health work.

While the work as a whole represents a contribution in a much needed field, it is impossible to avoid the feeling that a wider and closer knowledge of recent developments in medical economics might have improved the work and enabled the author to avoid many inaccuracies. There is a bibliography attached with comments that clearly show the bias of the author.

Manual of Medicine. By Sir Stanley Woodwark, C.M.G., C.B.E., M.D., Physician and Lecturer on Medicine, Westminster Hospital. Fourth edition. Cloth. Price, $5. Pp. 619, with illustrations. New York & London: Oxford University Press, 1935.

The author in one small volume discusses the following general subjects: diseases of the alimentary system, diseases of the kidneys, diseases of the respiratory organs, diseases of the circulatory system, diseases of the blood, the deficiency diseases, diseases of metabolism, diseases of the nervous system, and infectious diseases. In view of the fact that the book is intended to be a manual of medicine, the author has succeeded very well. In this edition he has made eliminations and additions. Under the subject of obesity, page 320, for example, he suggests the dietary treatment, pointing out numerous food articles that the patient should avoid, emphasizing regular systematic exercises, and closing with the statement that with due precautions thyroid, from 3 to 5 grains (0.2 to 0.3 Gm.) is given three times a day, especially if the basal metabolic rate is diminished. Fortunately, under the discussion of treatment he does not mention alpha-dinitrophenol.

Human Physiology. By F. R. Winton, M.D., Reader in Physiology, University of Cambridge, and L. E. Bayliss, Ph.D., Lecturer in Biophysics, University of Edinburgh. Foreword by C. Lovatt Evans, D.Sc., F.R.C.P., F.R.S., Jodrell Professor of Physiology and Fellow of University College, London. Second edition. Cloth. Price, $4.50. Pp. 627, with 221 illustrations. Philadelphia: P. Blakiston's Son & Co., Inc., 1935.

In this edition the same high standard of scientific accuracy and fundamental approach has been maintained as in the first. A good deal of material has been added, including many recent contributions to the subject. The sections on circulation, respiratory function of the blood, carbohydrate metabolism, muscle chemistry, the eye and the ear have been contributed to this edition by experts in these fields. Uniformity with the rest of the work has, however, been achieved, and there is a minimum of duplication. The bibliography is restricted to monographs and review articles in most instances. The book therefore is not of great use in looking up the literature of the subjects discussed. There is, however, an exceptionally complete index. Barring one or two of the more encyclopedic works, this is the most critical and reliable textbook now available for students of human physiology.

Die physiologischen und physikalischen Grundlagen der Hautthermometrie: Mit einem Anhang über weitere physiologische Temperaturmessungen. Von Priv.-Doz. Dr. med. H. Pfleiderer und Dr. phil. K. Büttner. Mit einem Geleitwort von Prof. Dr. A. Schittenhelm. Paper. Price, 4.80 marks. Pp. 52, with 10 illustrations. Leipzig: Johann Ambrosius Barth, 1935.

In view of the increasing practical importance of measurements of skin temperature, it is useful to have available in monograph form a rather critical analysis of the various methods in use, and a discussion of the influence of various environmental factors on skin temperature in normal and pathologic individuals. In the short treatment given, the references to clinical literature have been made brief and, in some respects, inadequate. The important underlying physical and physiologic principles have, however, been carefully outlined. The monograph should therefore be of interest and value to any one undertaking practical work involving skin temperature measurements.

Maimonides (The Rambam): The Story of His Life and Genius. By Dr. J. Münz. Translated from the German, with an introduction, by Henry T. Schnittkind, Ph.D. Octocentennial edition. Cloth. Price, $1.50. Pp. 238. Boston: Winchell-Thomas Company, 1935.

This gives in an interesting manner the story of the life and genius of the twelfth century philosopher, scholar and physician. Born in Cordova in 1135, Moses Ben Maimon was at 13 exiled from Spain through anti-Jewish persecution and, after traveling for a number of years in northern Africa and Palestine, settled finally in Egypt, where he became famous as a philosopher, teacher, writer, scholar, judge, astronomer, scientist, statesman, rabbi and physician. This book treats principally of his contributions to philosophy and rabbinic lierature. His principal works were "Mishneh Torah," a code and simplification of the Talmud, and "The Guide to the Perplexed," a philosophic treatise in which he aims to harmonize science, religion and philosophy. The chapter on Maimonides as a physician, although rather short, reveals to an extraordinary degree his thorough knowledge of the medical science of his time and deals with his contributions to dietetics, hygiene and treatment, many of which were far in advance of his time. The translator, as well as the author, have proved that the story of a medieval genius can be made as interesting as a present-day novel.

Précis d'histologie: La cellule, les tissus, les organes. Par A. Branca et J. Verne, professeurs à la Faculté de médecine de Paris. Cloth. Price, 65 francs. Pp. 631, with 420 illustrations. Paris: Masson & Cie, 1934.

This presents a concise description of the microscopic structure of the body. There are numerous black and white illustrations, the great majority being originals, some of which have been frequently borrowed by other authors from earlier editions of Branca's textbook. A better grade of paper would show them to better advantage. The text has been brought down to date and includes most of the important advances in histology and the attempts to correlate known functions with the minute

structure of the organs. Because of the relatively brief text, many questions are answered with a positiveness which does not reflect the actual state of existing knowledge. The new chapters on the living cell and the trends in histologic investigation are quite interesting. The volume constitutes a concise, accurate, modern textbook of histology.

Corazón y vasos. Por el Doctor Pedro Cossio, jefe de la sección cardiología del Instituto argentino de diagnóstico. Biblioteca de semiología para médicos generales y estudiantes. Boards. Pp. 385, with 266 illustrations. Buenos Aires: "El Ateneo," Librería científica y literaria, 1935.

The textbook Heart and Vessels was written for the medical student and the general practitioner. It is well printed, is accurately indexed, and contains many illustrations. The introduction contains the system of diagnosis and classification of heart disease advised by the American Heart Association. The material covered includes cardiac anatomy, physiology, pathology, history taking, examination of the cardiovascular system, and the various instrumental methods of cardiac investigation. The chapter on x-rays and electrocardiography are particularly well organized and illustrated. The material in the text is concisely and accurately written and meets the purpose for which the author designed the work.

Medicolegal

Malpractice: Injury to Ureter During Hysterectomy; Privileged Communications Statute Applicable to Patient in State Institution.—The physician-defendant performed a supravaginal hysterectomy on the plaintiff, removing the upper two thirds of the uterus. During this operation, the plaintiff claimed, the defendant negligently injured the left ureter, "resulting in causing an opening in said ureter above the bladder which now permits the urine . . . to pass . . . into the cervix stump where the injured portion of the ureter is now fastened, thence through the vaginal passage." Two operations performed by the defendant to correct the condition afforded no relief. In one of these operations, according to the plaintiff's charges, the intestine was lacerated, causing an opening through which gas and fecal matter passed uncontrolled into the vaginal passage and out with the urine. The patient sued the physician for malpractice. Shortly thereafter she was committed to a state institution for the insane and her guardian was substituted as party plaintiff. There was a judgment against the physician and he appealed to the Supreme Court of Kansas.

Evidence that shortly after the anesthetic was given in the first operation the physician-defendant threw a knife across the operating room was properly admitted, said the Supreme Court, as bearing on the question of negligence. During the trial a physician witness was asked whether, assuming certain facts to be true, the physician-defendant used the ordinary skill and care which surgeons practicing in the vicinity used in like operations. The witness replied: "Well, with these assumptions he did not." This testimony, said the court, did not trench on the province of the jury but was rather a statement of fact from which the jury might find negligence. The trial court did not err in refusing to permit two physicians on the staff of the state institution to testify. In Kansas, a physician may not testify, without his patient's consent, concerning any communication made to him in his professional capacity by his patient or concerning any knowledge obtained by a personal examination of the patient. By the great weight of authority, said the Supreme Court, the fact that a patient is an inmate of a state institution does not deprive the patient of the protection of the privileged communications statute with respect to any information acquired by a member of the professional staff of that institution in treating the patient. The defendant contended that the privilege of the statute, if any existed, was waived when the husband testified concerning the physical and mental condition of his wife. In holding that there had been no waiver, the Supreme Court relied on the case of *Metropolitan St. Ry. Co.* v. *Jacobi* (C. C. A.) 112 F. 924, wherein it was held that the fact that the plaintiff in an action for personal injuries introduces the testimony of physicians who attended him, with respect to the nature and extent of such injuries, does not operate as a waiver of the right to object to the testimony of another physician, called by the defendant, who had attended him for the same injuries, but at a different time. In the present case, continued the court, with the exception of a statement in a hypothetical question, that the patient had been confined in the state institution, there was nothing in the record concerning anything that happened at the institution.

For the reasons stated, the judgment in favor of the plaintiff was affirmed.—*Linscott v. Hughbanks (Kan.), 37 P. (2d) 26.*

Autopsies: Coroner's Right to Perform.—Kingsley was found dead in his car in a garage in Hennepin County, Minnesota. A deputy coroner of that county directed the undertaker, called by the deceased's wife to take charge of the body, to take the body to the county morgue. There the deputy coroner called a physician to perform an autopsy. The cause of death was found to be "monoxide gas poisoning." The wife was apparently not told that an autopsy was to be performed and did not learn of it until three weeks later. She then sued the deputy coroner, the undertaker, and the physician who performed the autopsy. A verdict was directed in favor of the defendants, and from an order denying a new trial, the plaintiff appealed to the Supreme Court of Minnesota.

A wife, said the Supreme Court, has a legal right to the possession of the dead body of her husband for the purpose of a decent burial and a wrongful mutilation of the corpse entitles her to damages against the wrongdoer. Her right, however, may be subjected to statutory regulation in the interest of public welfare. The coroner or deputy coroner of Hennepin county is required by statute to investigate all cases of "violent, mysterious and accidental deaths, including suspected homicides" and may order an autopsy when deemed proper. The death of the plaintiff's husband, said the court, undoubtedly came within the class of deaths the coroner was required by law to investigate and he had for the purposes of such investigation exclusive control of the body. The plaintiff contended, however, that an autopsy is authorized only as an incident to an inquest and that under the Minnesota law coroners may hold inquests "upon the dead bodies of such persons only as are supposed to have come to their death by violence." If, on investigation, the coroner deems a death accidental, he cannot hold an inquest. But, said the court, an autopsy may be the surest and most satisfactory way of determining that the death was accidental and, since the law provides that the coroner "shall order an autopsy when and where he deems proper," the conclusion is inescapable that the coroner may, as an aid to his investigation, order an autopsy. Furthermore, a coroner is required by law to make out a death certificate and to state therein the cause of death. To do so accurately, he may consider it necessary to have an autopsy performed. He may not arbitrarily order an autopsy when a properly conducted investigation has disclosed the cause of the death. It cannot be made to satisfy an idle curiosity or for the information of some interested insurance company.

The fact that the plaintiff was not informed that an autopsy was contemplated does not tend to prove an arbitrary exercise of the coroner's discretion. A public official is entitled to the presumption that in the performance of his duties he acts in good faith according to his best judgment. In the opinion of the court, the plaintiff's evidence was not sufficient to support a verdict that there was abuse of discretion in ordering an autopsy. A verdict was properly directed, therefore, in favor of the deputy coroner. Likewise, the undertaker was rightly entitled to a directed verdict, for, in taking the body to the morgue, he acted for the deputy coroner. The defendant physician who performed the autopsy must also, said the court, be held free from liability. Although the plaintiff contended that the autopsy went further than was necessary, the testimony was to the effect that it was performed in the usual way. It is almost self evident, said the court, that a proper autopsy to establish a cause of death not only should show a cause but should exclude all other supposable or possible causes. The plaintiff proved no excess mutilation nor any failure to replace

all organs examined, and the burden was on her to sustain the allegations of the complaint in respect to these matters.

The Supreme Court, therefore, affirmed the order of the trial court denying a new trial to the plaintiff.—*Kingsley v. Forsyth (Minn.), 257 N. W. 95.*

Malpractice: Negligent Treatment of Fracture.—The patient sustained a fracture of both bones of her right forearm, a comminuted fracture through the upper third of the ulna and a complete, oblique fracture through the neck of the radius. A deformity followed, with a 50 to 75 per cent limitation of motion in pronation and supination but with practically normal motion in flexion and extension. The patient sued the physician-defendant, and from a judgment in favor of the plaintiff for $5,950 the defendant appealed to the St. Louis court of appeals, Missouri.

The defendant complained of an instruction given by the trial court to the jury that the terms "carelessly" and "negligently" do not imply lack of skill or capacity but simply a disregard of ordinary care and caution; that if the jury found the defendant careless and negligent, the fact that the defendant may have been competent and skilful would not constitute a defense. This instruction, said the court of appeals, was correct. Malpractice may result either from injury occasioned by the physician's want of requisite knowledge and skill or from injury caused by the failure of the physician to exercise due care in the application of his skill and knowledge. The present case was founded solely on the theory of negligence and not on the theory of lack of knowledge and skill. Consequently, the question of lack of skill was not an issue in the case and his possession of the required skill, if he did not apply or use it, would constitute no defense.

During the trial the plaintiff called as an expert witness a physician whose office had been closed for twenty years but who had continued a small general practice. He had treated at least one fracture during that time. The defendant contended that this witness was not qualified to testify as an expert with respect to fractures. The court of appeals held that the witness was competent to testify, the limited scope of practice of the witness having a bearing only on the weight to be accorded his testimony.

In the opinion of the court, the verdict was excessive. A physician is liable only for the damage or injury caused by his malpractice and not for the results of the patient's original injury or illness. The plaintiff argued that if the fracture had been properly treated there would have been no ensuing impairment of function of the arm. There was medical testimony, however, that sometimes such fractures as those from which the patient suffered cannot be reduced regardless of the method of treatment adopted, and that such fractures are not commonly reduced in perfect apposition but only in useful apposition. In view of this testimony, the court believed that the verdict more nearly represented compensation for the patient's original injury than for the results of the physician's malpractice. Conditioned on the remittance by the plaintiff of the sum of $2,950, the court reversed the judgment of the trial court and remanded the case with directions to enter a judgment against the defendant for $3,000.—*Gunter v. Whitener (Mo.), 75 S. W. (2d) 588.*

Health Insurance: "Continuously and Actually Confined Within the House" Construed.—The defendant insurance company promised to pay certain benefits if the plaintiff suffered a confining illness, which required him to be "necessarily, continuously, and actually confined within the house, and therein regularly visited by a legally qualified physician." During the period from Jan. 20 to Dec. 3, 1931, the plaintiff underwent two operations to relieve a prostate involvement. He claimed that for the period named he was, within the meaning of the policy, continuously confined within his house. He obtained judgment under the policy in the trial court, and the insurance company appealed to the Supreme Court of Nebraska.

The insurance company conceded that the plaintiff had been continuously confined within his house from January 20 to March 26 but contended that thereafter he suffered a nonconfining illness. In support of this contention, the company presented evidence that on March 26 the plaintiff had been taken from his home to a bank, at which he had been bookkeeper, to explain certain matters to a depositors' committee, and that on a subsequent occasion he had again been taken to the bank on another matter. There was no contention that the removal of the plaintiff to a hospital and back to his home, on two occasions, broke the continuity of his confinement "within the house." The cases directly in point, said the Supreme Court, are hopelessly in conflict. The court, however, expressed itself as impressed with the following language used in *Garvin* v. *Union Mutual Casualty Co.,* 207 Iowa 977, 222 N. W. 25, 61 A. L. R. 633:

> "Strictly and continuously confined within the house," in its most literal interpretation, would require that the injured stay constantly within the four walls of the house. Such an interpretation would prevent recovery if an emergency, such as a fire, should arise, and the insured be removed from the house. It would preclude recovery in the event of transportation in an ambulance to a hospital, even for emergency treatment. It would bar recovery if the insured sat upon an uninclosed porch of the house, or slept upon a sleeping porch that was not "inclosed within the house." Such narrow and limited construction should not be adopted in the interpretation of contracts of this character.

In the present case, continued the court, the plaintiff was suffering from a serious illness. He suffered great pain, and hypodermics were frequently necessary during all this period. He was actually within the house except on the occasions noted and most of the time he was in a bed or on a couch. The seriousness of his illness is important only as throwing light on the question as to whether or not he was continuously confined. On the two occasions when the plaintiff was taken from the house, he performed no service except that of imparting to others information which was peculiarly within his own knowledge. The trips were made, not for his own interest or pleasure, but to assist others. To terminate his insurance under these facts would be to penalize him for making an extraordinary effort. The Supreme Court was unable to find any reversible error in the record and consequently affirmed the judgment of the trial court.—*Mackprang v. National Casualty Co. (Neb.), 257 N. W. 248.*

Society Proceedings

COMING MEETINGS

American Association of Railway Surgeons, Chicago, November 13-15. Dr. Louis J. Mitchell, 86 E. Randolph St., Chicago, Secretary.

American Clinical and Climatological Association, Princeton, N. J., Oct. 21-23. Dr. Francis M. Rackemann, 263 Beacon Street, Boston, Secretary.

American College of Surgeons, San Francisco, October 28-November 1. Dr. George W. Crile, 40 East Erie St., Chicago.

American Hospital Association, St. Louis, Sept. 30-Oct. 4. Dr. Bert W. Caldwell, 18 East Division Street, Chicago, Executive Secretary.

American Public Health Association, Milwaukee, Oct. 7-10. Dr. Reginald M. Atwater, 50 West 50th Street, New York, Executive Secretary.

American Roentgen Ray Society, Atlantic City, N. J., Sept. 24-27. Dr. E. P. Pendergrass, 3400 Spruce Street, Philadelphia, Secretary.

American Society of Tropical Medicine, St. Louis, November 19-22. Dr. Alfred C. Reed, 350 Post Street, San Francisco, Secretary.

Association of American Medical Colleges, Toronto, Canada, Oct. 28-30. Dr. Fred C. Zapffe, 5 South Wabash Avenue, Chicago, Secretary.

Association of Military Surgeons of the United States, New York, Oct. 3-5. Dr. H. L. Gilchrist, Army Medical Museum, Washington, D. C., Secretary.

Delaware, Medical Society of, Wilmington, Oct. 8-9. Dr. William H. Speer, 917 Washington Street, Wilmington, Secretary.

Indiana State Medical Association, Gary, Oct. 8-10. Mr. T. A. Hendricks, 23 East Ohio Street, Indianapolis, Executive Secretary.

Inter-State Postgraduate Medical Association of North America, Detroit, October 14-18. Dr. W. B. Peck, 27 E. Stephenson St., Freeport, Ill., Managing Director.

Kansas City Southwest Clinical Society, Kansas City, Mo., Oct. 7-10. Dr. Ralph R. Coffey, 1103 Grand Avenue, Kansas City, Mo., Secretary.

Kentucky State Medical Association, Louisville, Sept. 30-Oct.3. Dr. A. T. McCormack, 532 West Main Street, Louisville, Secretary.

Michigan State Medical Society, Sault Ste. Marie, Sept. 23-25. Dr. Burton R. Corbus, 313 Metz Building, Grand Rapids, Acting Secretary.

Nevada State Medical Association, Elko, Oct. 25-26. Dr. Horace J. Brown, 120 North Virginia Street, Reno, Secretary.

Ohio State Medical Association, Cincinnati, Oct. 2-4. Mr. C. S. Nelson, Hartman Theatre Building, Columbus, Executive Secretary.

Omaha Mid-West Clinical Society, Omaha, Oct. 28-Nov. 1. Dr. J. D. McCarthy, 107 South 17th Street, Omaha, Secretary.

Pacific Coast Society of Obstetrics and Gynecology, Los Angeles, Nov. 6-9. Dr. T. Floyd Bell, 400 29th Street, Oakland, Calif., Secretary.

Pennsylvania, Medical Society of the State of, Harrisburg, Sept. 30-Oct. 3. Dr. Walter F. Donaldson, 500 Penn Avenue, Pittsburgh, Secretary.

Southern Medical Association, St. Louis, November 19-22. Mr. C. P. Loranz, Empire Building, Birmingham, Ala., Secretary.

Virginia, Medical Society of, Norfolk, Oct. 15-17. Miss A. V. Edwards, 1200 East Clay Street, Richmond, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers to THE JOURNAL in continental United States and Canada for a period of three days. Periodicals are available from 1925 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Cancer, New York

24: 255-506 (June) 1935

Tumors of Neuromyo-Arterial Glomus. A. P. Stout, New York.—p. 255.
*Spindle Cell Epidermoid Carcinoma. H. E. Martin and F. W. Stewart, New York.—p. 273.
Phosphatase Activity of Tissues and Plasma in Tumors of Bone. C. C. Franseen and Regina McLean, Boston.—p. 299.
*Clinical Value of Prolan A Determinations in Teratoma Testis. M. Cutler and S. E. Owen, Hines, Ill.—p. 318.
Successful Irradiation Treatment of Eight Cases of Inoperable Rectal Carcinoma. B. F. Schreiner, Buffalo.—p. 326.
Delayed Metastatic Sarcoma of Pleura, Illustrating Diagnostic Value of Artificial Pneumothorax: Case. W. Bromme, H. P. Nelson and T. Findley Jr., Ann Arbor, Mich.—p. 334.
Primary Melanotic Sarcoma of Esophagus: Report of Case. T. C. Jaleski and P. V. Waldo, New York.—p. 340.
Giant Cell Tumor of Sacrum Which Invaded Inferior Vena Cava: Case. A. C. Freeman, K. K. Kinney and M. R. Moore, Norwich, Conn.—p. 345.
Glioma in Dog and Pinealoma in Silver Fox (Vulpes Fulvus). C. F. Schlotthauer and J. W. Kernohan, Rochester, Minn.—p. 350.
Growth Promoting and Growth Inhibiting Substances Extracted from Normal Organs: Experimental Study of Diet in Tar Cancer. J. Maisin and Y. Pourbaix, Louvain, Belgium.—p. 357.
Telecurie Therapy. B. F. Schreiner, M. C. Reinhard and W. H. Wehr, Buffalo.—p. 386.
Human Fibroblasts Grown for a Year in a Medium of Sheep Plasma and Two Solutions of Known Composition. Eleanor Erlichman, New York.—p. 393.
Cancer of Cervix Uteri in Nulliparous Women: Report of Fifty-Three Cases. P. Tompkins, Philadelphia.—p. 397.
*Hormone Origin of Uterine Fibroids: Hypothesis. J. T. Witherspoon, New Orleans.—p. 402.

Spindle Cell Epidermoid Carcinoma.—In the experience of Martin and Stewart, spindle cell carcinomas have not been radiosensitive. The heaviest doses of radon implants have failed to produce sterilization of the bed of the tumor and have permitted recurrences after the main bulk of the tumor has undergone radionecrosis. In many instances the local setting renders local excision by the scalpel a difficult or impossible procedure, owing to the scarred, inelastic and relatively avascular character of the tissues in which the tumors arise. In other cases the growth may be attached to underlying bone, and in these the actual cautery and endothermy at once suggest themselves as the most feasible method of surgical extirpation. In the authors' cases the use of these cautery methods has invariably been followed by local recurrence or by the development of a new tumor. It has seemed to them that, since the growth invariably arises in scarred tissues, any cautery method, by exciting the fibroblastic activity of the tissues, might be responsible for the development of an entirely new tumor in an area condemned to carcinogenesis, even though the one already existent has been destroyed. If the lesion is movable over underlying structures, surgical excision of the local tumor is undoubtedly the treatment of choice. All the patients now living and free of disease in the series of eight cases had wide local excisions. Local excisions failed to cure and were followed by repeated local recurrences in five cases and by metastases in three of these. If the growth infiltrates widely in the subcutaneous tissues, the authors recommend a far wider local removal than would be considered necessary in other forms of epidermoid carcinoma. Block dissection of the regional lymph nodes should be done if there are palpable metastases, although probably the procedure is of little value after metastasis has occurred. Prophylactic dissection of the regional lymph nodes seems to be both illogical and useless.

Follicle Stimulating Factor Determinations in Cases of Teratoma Testis.—Cutler and Owen made quantitative determinations of follicle stimulating factor (prolan A) on the urines of sixty-six patients suffering from teratoma testis. The amount of the substance varied between 50 and 16,000 mouse units. Thirteen normal men and patients suffering from benign lesions of the testicle were examined for follicle stimulating factor excretion in the urine. In all the amount was below 50 mouse units per liter of urine. The evidence supports the view that patients suffering from teratoma testis excrete about 50 mouse units of follicle stimulating factor per liter of urine, giving to this test a diagnostic value. In general, a marked diminution in follicle stimulating factor excretion following irradiation is accompanied by pronounced regression of the disease and an improvement in the general condition of the patient, whereas failure of the follicle stimulating factor to diminish or an increase in follicle stimulating factor excretion following treatment is paralleled by a failure to respond to therapy. Local recurrence is often preceded by a rise in the quantitative excretion of follicle stimulating factor in the urine, rendering the test of practical value in the follow-up control of this group of patients. The total twenty-four hour urine output should be determined and taken into consideration when the quantitative determination of follicle stimulating factor is estimated under conditions in which clinical conclusions are to be based on smaller variations, in order to avoid errors that might arise as the result of differences in fluid intake. A modification of Doisy and Katzman's benzoic acid method is presented, rendering the test more accurate in cases showing smaller quantities of follicle stimulating factor and preferable in cases in which the urine contains toxic products.

Origin of Uterine Fibroids.—Witherspoon offers pathologic and clinical evidence to support a hypothesis that there exists a cause and effect relationship between the unopposed and persistent action of the estrogenic principle produced by multiple follicle cysts of the ovaries, on the uterine endometrium and myometrium, and the production of (1) immediate endometrial hyperplasia and, provided the stimulation is sufficiently prolonged, (2) more latent uterine fibroids. Since this estrogenic principle affects the genital tract as a whole and also controls the development of the mammary glands, it would appear that this hormone stimulation is the initiating factor in the production of endometriomas and fibro-adenomas of the breast. He studied forty-four cases of endometrial hyperplasia. In each case a curettement was performed and the diagnosis made microscopically. In no case, either by bimanual examination or with the curet, was a uterine fibroid observed. In addition, in twenty of the cases a laparotomy was performed for other reasons. In no instance was a fibroid found, but multiple follicle cysts of the ovaries were observed in every case. After varying intervals, an average of four years and nine months, all forty-four patients returned for a second operation, this time for multiple uterine fibroids. The histologic observations in the endometrium, myometrium and ovaries are offered as evidence of an interrelationship between the multiple follicle cysts of the ovaries, endometrial hyperplasia and uterine fibroids.

American Journal of Clinical Pathology, Baltimore

5: 261-348 (July) 1935

Certification of Clinical Pathologists. F. H. Lamb, Davenport, Iowa.—p. 261.
Erythroblastosis in the New-Born and in Early Childhood. A. Yaguda, Newark, N. J.—p. 266.
Oral Glucose Tolerance Test: Review of Literature. G. B. Myers and R. M. McKean, Detroit.—p. 299.
Simple Method of Supplying Carbon Dioxide in Jars for Bacteriologic Cultures. L. Thompson, Rochester, Minn.—p. 313.
Reform in County Government and the Coroner's Office. O. T. Schultz, Evanston, Ill.—p. 316.
*Standardizing Sickle Cell Method and Evidence of Sickle Cell Trait. J. S. P. Beck and C. S. Hertz, Philadelphia.—p. 325.
Malignant Hemangioma. B. Markowitz, Bloomington, Ill.—p. 333.

Test for Demonstrating Sickle Cells.—Beck and Hertz describe a test for the demonstration of sickle cells, which consists of fixing the erythrocytes with formaldehyde after they have been allowed to assume their characteristic form in a test tube sealed with oil. It is also a convenient method for producing large numbers of sickle cells for demonstration purposes and for preparing permanent stained mounts. One or two drops of blood are collected in a test tube (4 by 1 cm.) containing physiologic solution of sodium chloride and 3 per cent solution of sodium citrate. The tube is inverted and the

mixture is shaken. It is covered with sufficient oil to make a layer 1 cm. thick. The preparation stands at room temperature for twenty-four hours, whereupon from 0.2 to 0.5 cc. of formaldehyde solution is introduced beneath the oil layer by means of the formaldehyde pipet. This is thoroughly mixed by forcing the liquids in and out of the pipet several times. The oil layer should not be broken for fear of letting air in too soon. Two or three minutes or more should be allowed for fixation. After this period the suspension is mixed again with the formaldehyde pipet to ensure a uniform distribution of cells. A few drops are removed from the tube, the excess oil is wiped from the tip and a drop is placed on a glass slide, covered and examined. The percentage is calculated in the manner of the differential leukocyte count. Permanent preparations are made from the suspension on coverglasses like an ordinary fresh blood film. The smears are dried in air and fixed by flame. Thirteen individuals with the sickle cell trait were found in a group of 100 Negroes examined by the sealed tube method, while only nine were found by the sealed smear method. In the nine sealed smear preparations, no observations were similar. The proportion of sickle cells in the series varied from 3 to 85 per cent, with an average of 26 per cent. In the tube preparations there were five instances of 98 per cent sickling, and in eleven of the thirteen cases the number of sickle cells varied between 85 and 99 per cent. The total number was more than four times that found in the same group by the slide method. The average for the thirteen cases was 77 per cent. Indeterminate cells were found more frequently in the slide preparations than sickle cells, and commonly in greater numbers. They were found in ten smear preparations and in only two tube preparations. The total number obtained by the slide method is more than five times as great as that found by the tube method. In nearly every slide preparation the number of erythrocytes was greater than that in the corresponding tube preparation of the same blood. The total number of apparently normal cells obtained by the slide method is more than twice that found by the tube method.

American J. Digestive Diseases and Nutrition, Chicago

2: 275-332 (July) 1935

Recent Development in Study of Oral Bacterial Flora. L. Arnold and C. W. Stuart, Chicago.—p. 275.
Gastroscopy: Past, Present and Future. E. Boros, New York.—p. 280.
New Tube for Anesthetization of Hypopharynx. R. Schindler, Chicago.—p. 281.
Symposium Concerned with Duodenal Factors in Neutralization of Acid Chyme. F. C. Mann and J. L. Bollman, Rochester, Minn.—p. 284.
Reaction of Content of Isolated Duodenum. P. R. Imes, Rochester, Minn.—p. 285.
Capacity of Duodenum to Neutralize, Buffer and to Dilute Acid. G. A. Stevens, Rochester, Minn.—p. 288.
Reaction of Duodenal Content After Exclusion of Bile from Duodenum. J. W. McRoberts, Rochester, Minn.—p. 293.
Effect of Exclusion of Pancreatic Secretion by Evulsion of Pancreatic Ducts on Reaction of Duodenal Content. M. T. Hoerner, Rochester, Minn.—p. 295.
Effect of Exclusion of Pancreatic Secretion by Pancreatic Fistula on Reaction of Gastric, Duodenal and Jejunal Contents. M. T. Hoerner, Rochester, Minn.—p. 298.
*Buffer Capacity of Pancreatic Juice. M. T. Hoerner, Rochester, Minn.—p. 300.
Peptic Ulcer Following Loss of Pancreatic Secretion Through Fistula: Experimental Study. M. T. Hoerner, Rochester, Minn.—p. 302.
Protection of Nutrition During Use of Elimination Diets. A. H. Rowe, Oakland, Calif.—p. 306.
Diaphragmatic Hernia: Report of Ten Cases of Esophageal Orifice Hernia. Katherine S. Andrews, Boston.—p. 310.
Use of Metal Clips in Gastro-Intestinal Anastomosis: Experimental Study. R. B. Bettman and L. M. Zimmerman, Chicago.—p. 318.

Buffer Capacity of Pancreatic Juice.—Hoerner experimented with the properties of the pancreatic juice collected from pancreatic fistulas. He titrated 1 cc. of the secretion with 1 cc. of tenth normal hydrochloric acid, a drop at a time, and the change in p_H with each minute addition was determined. Samples of pancreatic juice were collected at half-hour intervals during fasting and after the ingestion of protein, carbohydrate and fat test meals. The fluctuation in the buffering capacity during the eight-hour period of observation was determined. A continuous secretion of pancreatic juice was noted at all times, provided there was no infection or leakage present. Protein diets stimulated a greater flow of secretion than the other test meals used. The amount of secretion depended largely on the size of the animal and the kind and quantity of food ingested. The buffering capacity of the pancreatic juice reached its maximum from one to three hours after the ingestion of food and gradually diminished as the acidity in the duodenum decreased. The secretion was always alkaline and possessed slight buffering power during fasting. When the buffering capacity was highest, 1 cc. of pancreatic juice was capable of practically neutralizing an equal quantity of tenth normal hydrochloric acid.

Journal of Experimental Medicine, New York

62: 1-128 (July 1) 1935

Effect of Fasting on Serum Protein Concentration of Rat, with Especial Reference to Question of Existence of Immediately Utilizable Circulating Protein Fraction. H. C. Torbert, San Francisco.—p. 1.
Immunologic Specificity of Staphylococci: I. Occurrence of Serologic Types. L. A. Julianelle and C. W. Wieghard, St. Louis.—p. 11.
Id.: II. Chemical Nature of Soluble Specific Substances. C. W. Wieghard and L. A. Julianelle, St. Louis.—p. 23.
Id.: III. Interrelationships of Cell Constituents. L. A. Julianelle and C. W. Wieghard, St. Louis.—p. 31.
Degree of Dispersion of Bacillus as Factor in Infection and Resistance in Experimental Tuberculosis. R. M. Thomas and F. Duran-Reynals, New York.—p. 39.
Immunologic and Chemical Investigations of Vaccine Virus: I. Preparation of Elementary Bodies of Vaccinia. R. F. Parker and T. M. Rivers, New York.—p. 65.
Interstitial Bronchopneumonia: I. Similarity of Toxin Pneumonia to That Produced by Viruses. D. H. Sprunt, D. S. Martin and J. E. Williams, Durham, N. C.—p. 73.
Experiments on Epidemiology of Pseudorabies: I. Mode of Transmission of Disease in Swine and Their Possible Rôle in Its Spread to Cattle. R. E. Shope, Princeton, N. J.—p. 85.
Id.: II. Prevalence of Disease Among Middle Western Swine and Possible Rôle of Rats in Herd-to-Herd Infections. R. E. Shope, Princeton, N. J.—p. 101.
Effect of Anaerobically Prepared Pneumococcus Autolysate Toxin on Mice and Evaluation of Pneumococcus Autolysate Antitoxin in Mice. Julia T. Weld and Anne Gunther, New York.—p. 119.

American Journal of Hygiene, Baltimore

22: 1-256 (July) 1935

Influence of Solar Irradiation on Susceptibility of Mice to an Infection with Streptococcus Enteritidis. I. J. Kligler and L. Olitzki, Jerusalem, Palestine.—p. 1.
Course of Trypanosome Infection in Irradiated Rats. I. J. Kligler and R. Comaroff, Jerusalem, Palestine.—p. 11.
Culture of Mosquito Larvae Free from Living Micro-Organisms. W. Trager, Princeton, N. J.—p. 18.
Cultivation and Cross Infection Experiments with Balantidia from Pig, Chimpanzee, Guinea-Pig and Macacus Rhesus. E. C. Nelson, Baltimore.—p. 26.
*Study of Agglutinin Response to Typhoid Vaccine. Eugenia Valentine, W. H. Park, K. G. Falk and Grace McGuire, New York.—p. 44.
Immunity of Dogs to Ancylostoma Caninum. A. O. Foster, Baltimore.—p. 65.
Standardization of Photochemical Methods for Measurement of Solar Ultraviolet Radiation. H. S. Mayerson, New Orleans.—p. 106.
Calibration of Thermo-Integrator. C.-E. A. Winslow, A. P. Gagge, L. Greenburg, I. M. Moriyama and E. J. Rodee, New Haven, Conn.—p. 137.
Studies on Nature of Immunity to Intestinal Helminths: I. Local Nature of Immunity of White Rats to Nippostrongylus Infection. A. C. Chandler, Houston, Texas.—p. 157.
Immunity Against a Cestode Parasite, Cysticercus Pisiformis. K. B. Kerr, St. Louis.—p. 169.
Nose Opening Rays. L. Hill, London, England.—p. 183.
Relative Precipitin Response of Various Breeds of Rabbits: Possibility of Genetic Factor in Antibody Production. J. T. Culbertson, with assistance of J. F. Kent, New York.—p. 190.
Observations on Enzootic Paratyphoid Infection in Rat Colony. L. Buchbinder, L. Hall, S. L. Wilens and C. A. Slanetz, New York.—p. 199.
Rôle of Glycemic Response to Nicotine: Tobacco Smoking and Blood Sugar. W. J. McCormick, Toronto.—p. 214.
Purification and Culture of Tritrichomonas Foetus (Riedmüller) from Cows. R. W. Glaser and N. A. Coria, Princeton, N. J.—p. 221.
Diphtheria Antitoxin in Milk of Highly Immune Mother. J. Y. Sugg, New York.—p. 227.
Chicken Blood as an Immunizing Agent to Transplantable Rat Tumors. R. E. Gardner and R. R. Hyde, Baltimore.—p. 233.
Studies on Nature of Immunity to Intestinal Infections: II. Study of Correlation Between Degree of Resistance of White Rats to Nippostrongylus and Interval Between Infections. A. C. Chandler, Houston, Texas.—p. 243.

Agglutinin Response to Typhoid Vaccine.—According to Valentine and her associates, the rise in the agglutinin titers of the blood serums of rabbits and human beings, following the percutaneous administration of typhoid vaccine, paralleled the number of treatments and the size of the dose. The human subjects gave small rises in agglutinin titer after a large num-

ber of rubbings; the rabbits with a greater number of rubbings, larger doses and a relatively greater rubbing area gave good agglutinin titers. Intracutaneous injections of typhoid vaccine in weekly doses of 50, 100 and 150 million bacilli produced as great an agglutinin response as subcutaneous injections of 100, 200 and 300 million or 250, 500 and 1,000 million bacilli. Intracutaneous injections of 25, 50 and 100 million bacilli produced slightly less response. No appreciable systemic reactions and only slight to moderate local reactions followed the intracutaneous injections. Subcutaneous injections in doses of 100, 200 and 300 million bacilli, even 250, 500 and 1,000 million, produced some local and constitutional reactions, but much less than is commonly found with the standard subcutaneous doses of 500, 1,000 and 1,000 million. Oral administration of three different preparations of mixed typhoid-paratyphoid vaccines without preliminary bile treatment produced no significant rise in agglutinin titer when tested one month after ingestion. The results suggest the greater use of the intracutaneous method to obtain immunization.

American Journal of Surgery, New York

29: 171-336 (Aug.) 1935

Liver Abscess: Part I. Amebic Abscess; Analysis of Seventy-Three Cases. A. Ochsner and M. DeBakey, New Orleans.—p. 173.
Congenital Nonparasitic Single Cyst of Liver. E. A. Vander Veer, Albany, N. Y.—p. 195.
Ileostomy. D. P. MacGuire, New York.—p. 199.
Congenital Absence of Gallbladder. M. Danzis, Newark, N. J.—p. 202.
*Mesenteric Thrombosis (Arterial and Venous Types as Separate Clinical Entities): Clinical and Experimental Study. J. K. Donaldson and B. F. Stout, San Antonio, Texas.—p. 208.
Maternal and Fetal Mortality in the United States. H. J. Stander, New York.—p. 218.
Support of Pelvic Viscera and Mechanism of Prolapse. H. Koster, Brooklyn.—p. 226.
*Complete Procidentia in the Aged: Operative Treatment by Modified Lefort Technic. W. T. Liccione, Mount Vernon, N. Y.—p. 236.
Study of Diagnostic Errors in Four Years of Admissions to Gynecologic Service. M. J. Schreiber, New York.—p. 239.
Extra-Uterine Pregnancy Following Injection of Iodized Oil for Uterosalpingography: Etiology and Prevention Suggested: Report of Case. D. Polowe, Paterson, N. J.—p. 244.
Experimental Transplantation of Ovary: Autotransplants and Homotransplants of Dog Ovary into Omentum (Preliminary Report). G. H. Romberg, White Plains, N. Y.—p. 249.
Plastic Operation for Congenital Absence of Vagina. W. F. Wells, Atlanta, Ga.—p. 253.
Outline of Treatment for Various Types of Uterine Abortions. J. T. Witherspoon, New Orleans.—p. 256.
Primary Carcinoma of Lungs Combined with Pulmonary Tuberculosis. B. M. Fried, New York.—p. 261.
*Fatty Infiltration of Urinary Bladder with Spontaneous Rupture. O. Saphir and I. J. Shapiro, Chicago.—p. 263.
Fractures of Bones of Forearm: Discussion of Nonoperative Treatment and Report of One Hundred and Fifty Consecutive Recent Cases. V. Mooney, Pittsburgh.—p. 268.

Mesenteric Thrombosis.—Donaldson and Stout confine their remarks to the less clearly understood venous type. Since venous mesenteric thrombosis may occur as a complication of various conditions, the picture may be complicated by various pathologic elements. Generally, however, except in that type of venous mesenteric thrombosis initiated by sudden volvulus or intussusception, the onset and course would seem to be relatively slow and initiated by pains of a colicky nature. A striking symptom is the disproportion of the abdominal tenderness and the duration of symptoms to the abdominal rigidity. The abdomen is usually widely and definitely tender to deep palpation and the abdominal rigidity is not nearly as marked when the possible duration of the complaint and the definite tenderness are considered. The normal leukocyte relationship is moderately disturbed in the early stages but is markedly distorted later. An engorged intestinal wall may or may not be felt as a palpable mass. Occult blood is uniformly present in the stool and bowel movements continue, dark and soft to liquid in nature. Coffee ground-like vomitus may supervene. The temperature range in the uncomplicated picture is low. Intestinal obstruction, appendicitis, peritonitis, peptic ulcer, lead colic, simple enteritis, cholecystitis, gastritis and typhoid are among the diseases most likely to be confused by the expert. Arterial thrombosis is much more rapidly fatal than the venous type, which is probably compatible with recovery without surgery in a certain percentage of cases. The authors believe it is possible in a goodly number of cases to recognize mesenteric thrombosis and that the type, venous or arterial, may be identified at times preoperatively. They feel that a better understanding and closer inspection by the pathologist and the surgeon of cases of venous mesenteric thrombosis will lead to the more frequent pathologic diagnosis of hemorrhagic infarction of the intestine rather than to the diagnosis of "gangrene."

Complete Procidentia in the Aged.—Liccione is of the opinion that for complete procidentia in the aged no operation is as successful as that of Lefort. The prolapse must be reducible. If reducible, bed rest and topical applications will so soften the presenting mass as to reduce it. It is imperative to clear up all decubitus ulcers prior to operation so as to ensure primary union. Local or spinal anesthesia is preferable. The principle involved is the denudation and subsequent coaptation of rectangular areas on the anterior and posterior vaginal walls, respectively, thus creating a wide median supporting bar, above which rests the cervix. This bar is about 4 by 8 cm. in the average case and forms an effective support for the cervix and uterus. To each side of this median bar is a small canal, which is completely invested by vaginal mucosa and which carries off any cervical secretion. A high perineorrhaphy completes the operation and is a necessary part of it. A preliminary curettage is done to preclude fundal malignant changes. Erosion or ulcer of the cervix is taken care of by cautery or amputation.

Fatty Infiltration of Urinary Bladder.—Saphir and Shapiro observed fatty infiltration (lipomatosis) of the urinary bladder during the histologic examination of a patient who had died as a result of spontaneous rupture of this organ. The histologic sections revealed that muscle bundles had been replaced by fat tissue. The fatty infiltration was characterized by the formation of an abundance of subperitoneal fat, which extended into the musculature of the urinary bladder and occupied the usual position of the muscle fibers. Apparently the urinary bladder that is the seat of fatty infiltration may carry on its function as well as the normal urinary bladder but has little reserve power. The urinary bladder that is infiltrated by fat may rupture as a result of apparently insignificant causes. Fatty infiltration of the urinary bladder was found twice among thirty bladders examined.

Annals of Internal Medicine, Lancaster, Pa.

9: 1-114 (July) 1935

The Thyroid Stimulating Hormone of the Anterior Pituitary Gland. L. Loeb, St. Louis.—p. 13.
Present Status of Artificial Pneumothorax in Treatment of Lobar Pneumonia. S. S. Leopold and L. M. Lieberman, Philadelphia.—p. 19.
Agranulocytosis. H. Jackson Jr., Boston.—p. 26.
*Cyclic Agranulocytic Angina. D. J. Stephens and J. S. Lawrence, Rochester, N. Y.—p. 31.
Etiology and Prevention of Anemia in Pregnancy. M. B. Strauss, Boston.—p. 38.
Study of Nine Cases of Bronchomoniliasis. J. W. Flinn, R. S. Flinn and Z. M. Flinn, Prescott, Ariz.—p. 42.
Treatment of Acute Mercuric Chloride Poisoning. E. Hull and L. A. Monte, New Orleans.—p. 54
*"Eventration" of Right Diaphragm: Report of Case with Review of Literature, Chiefly from Standpoint of Etiology and Diagnosis. L. Feldman, I. M. Trace and M. I. Kaplan, Chicago.—p. 62.

Cyclic Agranulocytic Angina.—Stephens and Lawrence discuss a case of agranulocytic angina manifested by recurrences at the time of the menstrual cycles. Following bilateral oophorectomy there was a slight change in the picture during a period of one year, after which time no further recurrences occurred. Amidopyrine was taken at times by the patient, but the data do not allow any positive statement as to any causal relationship between it and the cycles of granulopenia. In order to determine whether menstrual periods in normal young women were associated with any comparable changes in the blood picture, the authors investigated the total and differential white blood cell counts of six women over a period of two months including two menstrual cycles. No variation greater than normal was present in the white blood cell counts. The bone marrow manifestations are of interest, since they presented a normal picture. The patient was able to respond to operation by the usual postoperative leukocytosis.

"Eventration" of Right Diaphragm.—Feldman and his associates add a case of right-sided "eventration" to the literature, thus raising the number of reported cases to ten. The diagnosis in the case was made because of the (1) high posi-

tion of the right diaphragm, (2) regular contour of the arched line as seen in the anteroposterior and lateral views, (3) definite, although limited, excursions of the elevated diaphragm, (4) roentgen observations after an opaque meal and after a barium sulphate enema, with the patient in the recumbent position, showing that the arched line was the dome of the diaphragm and not the outline of a distended intestine, and (5) evidence of inactivation of the right half of the phrenic leaf (Hoover's sign). The extruded intestine was situated between the right diaphragm above and the liver below. In this respect the case differs from the reported ones, in which it has been more usual to find the liver high up under the eventrated diaphragm. The patient has no intestine in the right side of the abdomen. Should she ever develop an attack of appendicitis, the symptoms would certainly be atypical and the method of surgical approach would have to be extraordinary indeed. The patient has been under observation for the last few years. She feels quite well. Should she become pregnant again, an abdominal section will be strongly urged before labor sets in.

Archives of Dermatology and Syphilology, Chicago

32: 181-362 (Aug.) 1935

Unusual Cutaneous Symptoms Associated with Retention of Arsenic. B. Throne and C. N. Myers, New York.—p. 181.
Lymphogranuloma Inguinale: Report of Case with Involvement of Retroperitoneal Lymph Nodes and Probable Involvement of Hip Joint, Adrenals and Kidneys, with Autopsy. H. S. Reichle and W. H. Connor, Cleveland.—p. 196.
Treatment of Paraffinoma: Report of Case. H. L. Baer, Pittsburgh. —p. 204.
Generalized Pustular Psoriasis: Report of Case. T. N. Graham, New York.—p. 208.
*Arsenic as an Etiologic Agent in Certain Types of Epithelioma: Differential Diagnosis from, and Further Studies Regarding, Superficial Epitheliomatosis and Bowen's Disease. H. Montgomery, Rochester, Minn.—p. 218.
Folliculitis Barbae Traumatica. S. S. Greenbaum, Philadelphia.—p. 237.
Mercury Inunctions. T. Sollmann, H. N. Cole and N. E. Schreiber, with collaboration of H. F. De Wolf and J. V. Van Cleve, Cleveland. —p. 242.
Eyelash Dye: Ill Effects and Some Problems Evoked by Them. H. Goodman, New York.—p. 258.
*Factors Affecting Color of the Skin: Their Significance in Berlock Dermatitis. J. R. Rogin and C. Sheard, Rochester, Minn.—p. 265.
Modified Composition of Iodobismitol: Results on Local Irritation. P. J. Hanzlik, C. W. Barnett and A. P. Richardson, with assistance of P. S. Pouppirt and M. R. Somers, San Francisco.—p. 284.

Arsenic and Epithelioma.—Montgomery states that arsenical keratosis must be regarded as potentially malignant and hence should be included among the precancerous types of dermatosis. Epitheliomas precipitated by arsenic are usually squamous cell epitheliomas, often with microscopic features simulating Bowen's disease, but usually the condition is graded 2 or 3, although clinically the course may not be as malignant as with ordinary squamous cell epitheliomas graded 2 or 3. Superficial epitheliomatosis is a relatively benign disorder, usually having a relatively benign course as compared with ordinary basal cell epithelioma. The treatment is surgical excision or excision by cautery. The lesions are prone to recur following radiotherapy.

Factors Affecting Color of Skin.—Rogin and Sheard made spectrophotometric analyses of the changes in color that took place in three areas of the skin which had been exposed to the same amount of irradiation from an air cooled quartz mercury vapor arc lamp. One area was moistened with oil of bergamot before being exposed to ultraviolet radiation; the second area was moistened with a 10 per cent alcoholic solution of oil of bergamot before irradiation, and the third was treated only by irradiation and thus served as a control. The area used as a control also gave information regarding the course of erythema and pigmentation in the normal skin after ultraviolet irradiation. They found that the use of the spectrophotometer affords an accurate method of recording the changes of color in the skin after ultraviolet irradiation. The initial erythematous reaction of the skin is generally crisis-like in form, but it may also be plateau-like or double crisis-like. The course of the erythema is rhythmic or wavelike in nature and persists over a period of weeks. In the same subject the amount of pigment formed after ultraviolet irradiation is proportional to the degree of the preceding erythema. This statement cannot be made, in the light of the data at hand, when erythema and pigmentation are compared in different patients after ultraviolet irradiation. The changes in pigment follow a rhythmic course, apparently independent of the course of erythema. There are marked individual variations in the chronology of the waves, which appear during the course of erythema and pigmentation. The hue of the skin after ultraviolet irradiation remains constant. The changes in the redness of the skin after ultraviolet irradiation are due to changes in purity (saturation) of the hue. The presence of chlorophyll in solutions of oil of bergamot was shown by obtaining curves for spectrophotometric transmission that are characteristic of chlorophyll. There was a decrease in the spectrophotometric transmission of solutions of oil of bergamot after ultraviolet irradiation. Oil of bergamot and a 10 per cent alcoholic solution of oil of bergamot applied to the skin before ultraviolet irradiation diminish the effects of such irradiation. Ultraviolet irradiation following applications of oil of bergamot and a 10 per cent alcoholic solution of oil of bergamot to the skin did not produce dermatitis or increased pigmentation in any of the cases studied. The authors suggest that berlock dermatitis belongs to the group of cutaneous reactions of the venenata type and that it is due to an individual hypersensitivity to chlorophyll or adulterants found in the perfume or toilet water that has been applied to the skin.

Archives of Neurology and Psychiatry, Chicago

34: 243-480 (Aug.) 1935

Juvenile Dementia Paralytica: IV. Syndromes of Cranial Nerves and Motor System. W. C. Menninger, Topeka, Kan.—p. 243.
Insulin in Catatonic Stupor. Charlotte Munn, Orangeburg, N. Y. —p. 262.
Perceptual Basis of Somatic Delusions in Case of Schizophrenia. A. Angyal, Worcester, Mass.—p. 270.
Some Signs of Organic Disorder in Schizophrenia. P. B. Marquart, Lane, Kan.—p. 280.
Method for Investigating Fantasies: Thematic Apperception Test. Christiana D. Morgan and H. A. Murray, Cambridge, Mass.—p. 289.
Psychologic and Physiologic Phenomena During Prolonged Vigil. S. E. Katz and C. Landis, New York.—p. 307.
Involuntary Graphic Sprawl: Motor Phenomenon Related to Mirror Writing and Modified by Factor of Handedness. C. Quinan, San Francisco.—p. 318.
Observations on Experimental Neurosis in Sheep. O. D. Anderson and H. S. Liddell, Ithaca, N. Y.—p. 330.
Moulages: Their Preparation and Service to Neuropathologist. J. H. Globus, New York.—p. 355.

Arkansas Medical Society Journal, Fort Smith

32: 47-60 (Aug.) 1935

Fractures Involving the Elbow Joint. V. Parmley, Little Rock.—p. 47.
Goiter, a Preventable Disease: Short Review of Its Medical and Surgical Aspects. E. M. Holder, Memphis, Tenn.—p. 51.

Canadian Medical Association Journal, Montreal

33: 1-124 (July) 1935

The Breath of Life. J. C. Meakins, Montreal.—p. 1.
Nutrition and the Future of Man. J. S. McLester, Birmingham, Ala. —p. 6.
Vagal and Phrenic Impulses and Respiration. Ruth C. Partridge, Toronto.—p. 11.
Maduromycosis: Report of Case Due to Monosporium Apiospermum. R. M. Shaw and J. W. Macgregor, Edmonton, Alta.—p. 23.
*Monosporium Apiospermum, Fungus Causing Madura Foot in Canada. Eleanor Silver Dowding, Edmonton, Alta.—p. 28.
Focal Epileptic Discharge in Case of Tumor of Posterior Temporal Region. W. Penfield, Montreal.—p. 32.
Bronchial Stenosis in Pulmonary Tuberculosis. C. H. Andrews, Prince Albert, Sask.—p. 36.
Early Protected Weight Bearing in Treatment of Fractures of Foot, Ankle and Leg. F. B. Gurd, Montreal.—p. 41.
*Comparative Tendency of Kraurosis and Leukoplakia of Vulva to Become Malignant. P. J. Kearns, Montreal.—p. 48.
Clinical and Pathologic Features of Series of Twenty Cases of Hodgkin's Disease. E. S. Mills and J. E. Pritchard, Montreal.—p. 50.
Acute Cholecystitis. J. McKenty, Winnipeg, Manit.—p. 59.
The Antipyretics. V. E. Henderson, Toronto.—p. 64.
Physiopathology of Simultaneous Bilateral Pneumothorax. A. M. Cholette, Montreal.—p. 67.

A Fungus Causing Madura Foot in Canada.—Dowding has grown Monosporium apiospermum, which has been isolated for the first time in Canada, on culture mediums and has made a comparison with cultures of the same fungus obtained from Europe. In addition to characters described previously she has observed the following features: 1. The cultures darken from white to cinnamon drab. Unlike the strains obtained in the

United States, they produce no sclerotiums. They frequently exhibit a growth of short dark brown aerial hyphae. 2. The mycelium is characterized by terminal and intercalary swellings and "racquet hyphae" resembling the growth forms of many dermatophytes. 3. The form of the conidiophores depends on their habit of growth; when they are submerged in the medium they are undifferentiated from the other hyphae; when they are growing in the air they become erect, tapering and dark colored. 4. The sterigmas sometimes occur on the conidiophores in whorls of from two to five. 5. The spores are normally borne singly, but sometimes they collect in groups, when a sterigma produces several spores in succession. Geomyces sp., isolated from Alberta soil, resembles certain fungi causing maduromycosis, but it was found not to be pathogenic to an experimental guinea-pig.

Kraurosis and Leukoplakia of Vulva.—During the last eight years Kearns observed seventeen cases of carcinoma of the vulva, fourteen of which were sectioned and treated. Four of these showed a definite origin in leukoplakia. The chief clinical symptom in all cases of leukoplakia was pruritus, whereas in kraurosis the chief complaints were of dyspareunia, soreness and bleeding, and in carcinoma of a tumor of the vulva, with pain and bleeding. It is his belief that all cases of kraurosis vulvae have a previous hypertrophic or leukoplakic stage, and if this hypertrophy is prolonged a progressive leukoplakia will develop, which will go through the stages of metaplasia and cancer formation. If, however, atrophy ensues the leukoplakia progressively gives rise to kraurosis, and the involved skin becomes thinner and thinner, resembling parchment. The surface becomes dry, scarlike and brittle. The shrinkage in this cicatricial sclerotic tissue produces a stretching of the skin over the nymphae. The latter may entirely disappear, as may also the frenulum of the clitoris. The vestibule of the vagina becomes funnel shaped and narrow, causing dyspareunia and pain on examination, because the diseased skin is easily torn and fissured. Histologically, kraurosis shows an atrophy in all layers of the epidermis, especially of the horny layer and the lowest layer. A complete loss of the papilla of the cutis occurs, allowing the epidermis and cutis to lie in flat adjacent layers. In the outer and reticular layers of the corium, in contrast to the edema of leukoplakia, a homogeneous hyalinized material is seen, which spreads diffusely throughout the subcutaneous tissue, fat, elastic fibers, hair follicles, glands of the hair follicles, sebaceous glands and sweat glands. These structures gradually disappear. If large sections are taken through the vulva, these atrophic changes can be seen and connected with remnants of leukoplakic areas. In the hypertrophic or leukoplakic stage pruritus is a common symptom, but in the atrophic stage or kraurosis, soreness and bleeding are the troublesome features. The symptoms of pruritus may be relieved by resection of the perineal nerves in the vulva, causing anesthesia of the part; but this may obscure hypertrophic changes developing. Painting the surface with a 5 per cent solution of silver nitrate often gives relief. The administration of ovarian extract may help. If the leukoplakic stage persists, resection of the vulva should be done, as from 20 to 25 per cent of persistent leukoplakias will become malignant.

Canadian Public Health Journal, Toronto

26: 315-366 (July) 1935

Provision of Medical Care in Western Canada. F. W. Jackson, Winnipeg, Manit.—p. 315.
Evaluation of Health Hazards in Industry. F. M. R. Bulmer, Toronto.—p. 321.
Basis for Control of Tuberculosis in Defined Area. C. G. Shaver, St. Catharines, Ont.—p. 329.
Contributions to Laboratory Diagnosis of Amebiasis from the Chicago Outbreak of 1933. F. O. Tonney, Marian McIlhenny, G. L. Hoeft and C. H. Koonz, Chicago.—p. 335.

Colorado Medicine, Denver

32: 593-688 (Aug.) 1935

The Common Cold. C. E. Harris, Woodmen.—p. 604.
The Apple Diet in Treating Diarrhea in Infants and Children. H. B. Stein, Denver.—p. 608.
Automobile Injuries and Comparative Death Rates, with Some Suggestions as to Their Treatment in "Traumatic Surgery." C. W. Streamer, Pueblo.—p. 612.
Value of Red Cell Sedimentation Test, with Especial Reference to Pulmonary Tuberculosis. A. R. Masten, Wheat Ridge.—p. 615.

Endocrinology, Los Angeles

19: 383-508 (July-Aug.) 1935

Clinicopathologic and Experimental Study of Functional-Structural Relationship of Goiter. J. Rabinovitch, J. R. Pearson and H. W. Louria, Brooklyn.—p. 383.
Some Factors Influencing Lengths of Survival Following Bilateral Suprarenalectomy. E. D. Sisson and B. March, Minneapolis.—p. 389.
Cow's Milk as Possible Excretory Source of Anterior Pituitary-like Hormone. A. I. Weisman, I. S. Kleiner and E. Allen, New York.—p. 395.
Idiopathic Hypoparathyroidism and Tetany in Fowl. F. B. Hutt and W. L. Boyd, St. Paul.—p. 398.
*Endocrine Origin of Primary Dysmenorrhea and Its Hormone Treatment: Preliminary Report. J. T. Witherspoon, New Orleans.—p. 403.
Corpus Luteum of Pregnancy in Relation to Anterior Pituitary Gland. M. Feresten, New York.—p. 407.
Study of Effects of Intermedin and Injury of Hypophysis on Traumatic Corial Melanophores in Goldfishes. G. M. Smith, H. S. Burr, R. S. Ferguson, New Haven, Conn., and New York.—p. 409.
Effects of Pregnancy Urine Administration to Female Swine. E. P. Tschernozatonskaja, Moscow, U. S. S. R.—p. 413.
Effect of Injection of Residual Ovarian Extracts. H. W. Marlow and F. Groetsema, Manhattan, Kan.—p. 415.
Relation of Contracture and Tetany to Experimentally Produced Calcium Deficiency in Cats, With and Without Lesions of Cortical Motor Areas. Helen C. Coombs, F. H. Pike and D. S. Searle, New York.—p. 421.
Diuresis Associated with Direct Stimulation of Hypophysis. W. R. Ingram and R. W. Barris, Chicago.—p. 432.
Castration Atrophy and Theelin: Effect of Theelin on Atrophic Uteri of Castrated Albino Rats. B. L. Robinson and W. C. Langston, Little Rock, Ark.—p. 441.
Study of Response of Heart to Pitressin Following Administration of Thyroid Extract. C. M. Gruber, V. H. Moon and E. Sufrin, Philadelphia.—p. 447.
Relation of Diet and Serum-Calcium to Tetany in Parathyroidectomized Rat. Margaret M. Hoskins, New York.—p. 453.
*Studies in Thrombo-Angiitis Obliterans (Buerger) X: Reduction in Blood Volume Following Bilateral Oophorectomy. Mae Friedlander, N. Laskey and S. Silbert, New York.—p. 461.
Experimental Hypertrophy and Atrophy of Prostate Gland. D. R. McCullagh and E. L. Walsh, Cleveland.—p. 466.
Quantitative Studies on Reaction of Anterior Pituitaries of Immature Female Rats to Extracts of Pregnancy Urine. J. M. Wolfe, Nashville, Tenn.—p. 471.

Endocrine Origin of Primary Dysmenorrhea.—Witherspoon points out that the most recent explanation of primary dysmenorrhea is an endocrine imbalance. Reynolds has shown that uterine rhythmic contractions become increasingly more active as the graafian follicle develops. After rupture of the follicle and corpus luteum formation, the uterine contractions are inhibited. The pain of primary dysmenorrhea can be explained by the withdrawal of the progestin influence, which results in whipping into marked activity, by the action of the follicular hormone, a uterus that has been lying in a quiescent state for from ten days to two weeks. The rationale of treatment in this condition is to counterbalance the follicular hormone activity by administering the luteinizing principle found in the urine of pregnant women. The method of treatment employed was to inject intramuscularly and daily 250 rat units of gonadotropic principle of pregnancy urine (follutein-Squibb) from three to four days previous to the expected flow and from one to two days during the flow. Thirteen of seventeen patients so treated for dysmenorrhea experienced relief.

Thrombo-Angiitis Obliterans.—Friedlander and her associates determined the significance of the blood volume in thrombo-angiitis obliterans in twenty-five patients who had had a surgical removal of both ovaries and the uterus, and a control group of twenty-one patients. In addition, a number of female cats were subjected to bilateral oophorectomy. The cholesterol, fibrinogen and viscosity were selected as factors that might have a bearing on the greater tendency to thrombosis. The average blood volume in the oophorectomized cases showed a reduction of about 25 per cent from the normal. This change became more striking after the first few months. Coincident with this there was an elevation of the cholesterol and fibrinogen of the plasma and an increase in viscosity of the blood. There was a consistent tendency for the cholesterol figures to be higher and they were supported by a diminished blood volume. A normal blood volume was obtained in only one patient who had had a bilateral oophorectomy, who presented a definite clinical picture of hyperthyroidism with a basal metabolism of plus 47 per cent. In the control group all the blood volume figures

were within normal limits and the cholesterol, fibrinogen and viscosity were correspondingly lower. This group included eleven patients with normal menopause and artificial menopause produced by radiotherapy. It would appear, therefore, that some substance capable of influencing the blood volume is produced by the ovaries even after other physiologic functions have ceased. The cats subjected to operation showed a consistent tendency toward a reduction in blood volume after bilateral oophorectomy. In one animal, in which only a single ovary was removed, there was no reduction in volume.

Florida Medical Association Journal, Jacksonville

22: 1-48 (July) 1935

*Friedman Test for Pregnancy: Report of Two Hundred and Thirteen Cases. H. R. Mills, Tampa.—p. 11.

Tuberculosis and the General Practitioner. W. A. Claxton, Jacksonville.—p. 22.

Proper Evaluation of Psychic Element in Medical and Surgical Practice. S. A. Shoemaker, Orlando.—p. 24.

Friedman Test for Pregnancy.—Mills presents 213 cases in which the Friedman test was used, of which 96.7 per cent have been proved correct by subsequent clinical events. His experience shows that a certain number of false positive results can be avoided by not using rabbits that gave positive results before. A certain number of false negative results can be avoided by not laparotomizing the rabbit but by killing the animal and exposing the ovaries with wide dissection. A certain number of false negative reactions can be avoided also by obtaining a concentrated first morning voiding. If a test should prove negative in a patient who has passed a regular menstrual period only a day or so, it must be borne in mind that the patient may be less than two weeks pregnant and the test should be repeated at a suitable interval. A certain number of errors can be avoided also by examining the ovaries of the rabbit by microscopic section. The test has proved useful in the diagnosis of early pregnancy and differentially in fifteen cases of menopause; seven ovarian cysts, including one dermoid cyst, one lutein cyst, one endometrial cyst or chocolate cyst, two pseudomucinous cystadenomas and two cysts of unknown type; two cases of acute pus tubes; three myofibromas of the uterus, and one case of chronic epididymitis (all of which were negative); also in suppressed, delayed and irregular menses, fear of pregnancy and one case of attempted blackmail. One case of chorionepithelioma was positive. The Friedman test, like all other single diagnostic methods, should not be relied on exclusively in the diagnosis of pregnancy or other conditions but should be employed only in correlation with a careful physical examination and clinical history of the case.

Johns Hopkins Hospital Bulletin, Baltimore

57: 1-46 (July) 1935

Rôle of the Nurse in the Control of Tuberculosis. W. H. Welch.—p. 1.

*Effects of Intravenous Administration of Hypertonic Solutions of Sucrose, with Especial Reference to Cerebrospinal Fluid Pressure. J. H. Masserman, Baltimore.—p. 12.

Syphilitic Myocarditis. T. P. Magill, Baltimore.—p. 22.

Studies on Virus Problems: III. Elementary Bodies in Virus Infections and Filtrable Avian Tumors and Their Etiologic Significance: Outlook for the Future. J. C. G. Ledingham, London, England.—p. 32.

Hypertonic Solutions of Sucrose.—In an attempt to find a nontoxic substance the osmotic action of which in the circulation would not be complicated by adverse sequels, Masserman investigated the physiologic effects of the intravenous injection of hypertonic solutions of sucrose in thirty-five human subjects. He found that a 50 per cent solution of sucrose is satisfactory for clinical use. When from 300 to 500 cc. of this solution is administered intravenously, the initial rise of cerebrospinal fluid pressure is of lesser degree and duration than is the case with the dextrose or the electrolytic solutions. Subsequently the desired diminution in intracranial tension is greater and more prolonged. Corresponding to the relative impermeability of the blood-cerebrospinal fluid barrier to sucrose there is only a slight and transient intracranial hypertension as the final hydrodynamic effect of its intravenous administration. In contrast to this, dextrose and most of the physiologic solution of sodium chloride pass readily from the blood into the central nervous system and the cerebrospinal fluid and thereby induce a marked and prolonged increase in spinal fluid pressure and possibly also an edema of the central nervous tissues. The 50 per cent solution of sucrose when administered intravenously does not cause an overt phlebitis in the injected vein and induces only a mild reaction if allowed to escape in small amounts into the subcutaneous tissues. Comparatively large amounts of sucrose in the circulation are apparently not toxic and cause no serious disturbances in the chemistry or cytology of the blood. Being a disaccharide and foreign to the blood stream, sucrose induces a marked diuresis and is eliminated rapidly in the urine. Since sucrose is thus either completely eliminated or else metabolized in the body only in small amounts, repeated injections may be given when necessary without cumulative adverse effects. As to the clinical use of hypertonic solutions of sucrose for the purpose of reducing the intracranial hypertension in patients with cerebral concussion, in meningitis, and preoperatively in cases of brain tumor, the author states that it must be recognized that the disturbances in cerebral circulation and tissue permeability that obtain in these conditions might modify the osmotic and dynamic effects that he reports in normal subjects. Nevertheless, in view of the ready availability and apparent lack of toxicity of the solutions, their administration for their demonstrated decompressive and diuretic effects seems to deserve a careful clinical trial.

New England Journal of Medicine, Boston

213: 91-134 (July 18) 1935

Dislocations. W. E. Gallie, Toronto.—p. 91.

Reticulocyte Response in Guinea-Pigs Following Oral Administration of Certain Antianemic Substances. D. K. Miller and C. P. Rhoads, New York.—p. 99.

Early Classification and Early Diagnosis of Cancer of Bronchus, with Analysis of Thirty-One Case Reports, Including Three Pathologic Diagnostic Errors. M. S. Lloyd, New York.—p. 101.

Combined Extra-Uterine and Intra-Uterine Pregnancy: Report of Two Cases. R. J. Heffernan, Boston.—p. 120.

Case Report: Bronchial Asthma Due to Paper Sensitivity. T. Bennett, Boston.—p. 121.

213: 135-194 (July 25) 1935

Sensitivity to Environmental Allergens in Infantile Eczema. L. W. Hill, Boston.—p. 135.

Traumatic Chondromalacia of Patella: Report of Two Cases. F. A. Slowick, Pittsfield, Mass.—p. 160.

Recent Advances in Treatment of Rectal Diseases by Injection Methods in Ambulatory Patients: I. Use of Gabriel's Modified Solution in Treatment of Fissure-in-Ano. N. Steinberg, Boston.—p. 162.

Etiology of Congenital and Hereditary Deformities. S. M. Fitchet, Boston.—p. 164.

*The 'Phthalein Test of Kidney Function in Anemia. E. M. Chapman, Boston.—p. 166.

Jacob Zahalon, and His Book, "The Treasure of Life." H. A. Savitz, Boston.—p. 167.

Low-Back Pain Caused by Lumbosacral Abnormalities. M. N. Bellerose, Rutland, Vt.—p. 177.

Phenolsulphonphthalein Test of Kidney Function in Anemia.—Chapman investigated eleven cases of severe anemia that showed no signs of cardiovascular or renal disease. The urine in each case was normal. A fractional phenolsulphonphthalein test of kidney function was done on each patient. The patient emptied the bladder and drank 400 cc. of water, and half an hour later 1 cc. of phenolsulphonphthalein was injected intravenously. Specimens of urine were then obtained fifteen, thirty, sixty and 120 minutes after the injection. The first two collections show the high initial output of dye, which is the significant feature of phenolsulphonphthalein excretion. The curve of elimination of dye was normal in each case. Anemia alone does not affect the excretion of phenolsulphonphthalein by the kidneys.

New Orleans Medical and Surgical Journal

88: 1-72 (July) 1935

1934-1935 Memorial Address of the Louisiana State Medical Society. J. T. Nix, New Orleans.—p. 1.

Louisiana System of Hygienic Public Education. F. J. Mayer, Opelousas.—p. 10.

Importance of Mental Hygiene to the General Practitioner. T. J. Perkins, Simmesport.—p. 16.

Effectiveness of Typhoid Vaccine in Control of Typhoid Fever. R. W. Todd, New Orleans.—p. 19.

Who Is to Blame for Cancer Deaths? W. H. Perkins, New Orleans.—p. 25.

Toxoid Immunization: New Orleans Campaign for Diphtheria Eradication. J. Signorelli, New Orleans.—p. 30.

Public Health Reports, Washington, D. C.

50: 891-908 (July 5) 1935

Malaria Epidemic in Aurora, Ohio. R. N. Hoyt and R. D. Worden.—p. 895.

50: 909-922 (July 12) 1935

Tularemia: Observations on Strain of Low Initial Virulence from Rabbit Ticks. C. B. Philip and G. E. Davis.—p. 909.

50: 923-948 (July 19) 1935

Bubonic Plague on the West Coast of South America in 1934. J. D. Long.—p 923.

Rhode Island Medical Journal, Providence

18: 93-110 (July) 1935

Address: Early Medical History in Rhode Island and the Rhode Island Medical Society. W. L. Munro, Providence.—p. 93.

18: 111-128 (Aug.) 1935

Electrocardiogram in Diagnosis of Heart Disease. F. B. Cutts, Providence.—p. 111.

Surgery, Gynecology and Obstetrics, Chicago

61: 145-288 (Aug.) 1935

Irregular Shedding and Irregular Ripening of Endometrium. H. F. Traut and Alberta Kuder, New York.—p. 145.

*Fundusectomy in Treatment of Peptic Ulcer: Experimental Study. H. Seely and R. Zollinger, Boston.—p. 155.

Peptic Ulcer and Anxiety Complex: Failure of Pharmacologically Sustained Hypersecretion and Hypermotility of Stomach to Produce Chronic Gastric Ulcer in Dogs. J. R. Orndorff, G. S. Bergh and A. C. Ivy, Chicago.—p. 162.

Roentgenkymograph as New Aid in Diagnosis of Adhesive Pericarditis. S. E. Johnson, Louisville, Ky.—p. 169.

*Evidence for Placental Origin of Excessive Prolan of Late Pregnancy Toxemia and Eclampsia. G. Van S. Smith and O. W. Smith, Brookline, Mass.—p. 175.

Lateral Approach for Operating on Diverticula of Bladder. D. R. Melen, Rochester, N. Y.—p. 184.

Treatment of Congenital Clubfeet. J. H. Kite, Decatur, Ga.—p. 190.

Congenital Deformities of Face: Types Found in Series of One Thousand Cases. W. B. Davis, Philadelphia.—p. 201.

Foreign Bodies in Stomach: Removal by Peroral Endoscopy. L. H. Clerf, Philadelphia.—p. 210.

Thrombo-Angiitis Obliterans (Buerger) XI: Treatment of Five Hundred and Twenty-Four Cases by Repeated Intravenous Injections of Hypertonic Salt Solution: Experience of Ten Years. S. Silbert, New York.—p. 214.

Jejunal Diverticulosis. R. S. Rosedale, Buffalo.—p. 223.

Primary Neoplasms of Female Urethra. J. G. Menville, Rochester, Minn.—p. 229.

Knee Flexion Contracture Treated by Skeletal Traction. G. E. Haggart, Boston.—p. 239.

*Granulosa Cell and Brenner Tumors of Ovary: Report of Case with Review of Those Cases Already Recorded. P. B. Bland and L. Goldstein, Philadelphia.—p. 250.

Fundusectomy in Treatment of Peptic Ulcer.—Seely and Zollinger resected the gastric fundus from four dogs, leaving a tube about 3 cm. in diameter from the esophageal opening to within 6 cm. of the pylorus. This tube was made up chiefly of gastric mucosa, smooth and free of rugae. An immediate postoperative drop of both free and total acidities was found, as compared to the preoperative levels. There was a gradual return of the free and total acid, reaching preoperative levels by the end of eight months. The stomach at necropsy showed hypertrophy to normal size and outline, without reproduction of rugae. Microscopic examination of the postoperative stomachs showed a rich distribution of active acid bearing cells, especially along the greater curvature. Histologically these cells were filled with secretory granules and vacuoles, suggesting that they were actively forming hydrochloric acid. The experimental studies agree with the clinical observation that the gastric acidity cannot be permanently lowered regardless of the amount of acid bearing tissue removed. Fundusectomy has little to offer as a means of permanently reducing gastric acidity and as a possible therapeutic measure in the control of peptic ulcer.

Origin of Excessive Anterior Pituitary-like Principle of Eclampsia.—The Smiths' quantitative analyses of the serum and urine for anterior pituitary-like principle and estrogenic substance in a series of sixty-eight women in the second half of pregnancy have shown that late pregnancy toxemia and eclampsia are characterized almost without exception by a marked excess of anterior pituitary-like principle as compared with normals. A low level of estrogenic compound in a large proportion of these patients has also been found, but the quantitative abnormality of this hormone is less striking and less consistent than that of anterior pituitary-like principle. Both the placenta and the anterior lobe of the hypophysis are known to contain gonadotropic factors. The authors' experiments were carried out for the purpose of determining which of these two sources is responsible for the excess found in late pregnancy toxemia and eclampsia. The serums of women with late pregnancy toxemia and eclampsia have been found to have the same effect on the ovaries of hypophysectomized rats as the serums of normally pregnant women. An extract of human placenta also had this effect, while hypophyseal anterior pituitary-like principle caused a follicular and luteal activity not caused by any of the other materials tested. The placentas of toxemic and eclamptic patients contain excessive amounts of anterior pituitary-like principle and tend toward low levels of estrogenic material as compared with the placentas of normal pregnancies. Control tissues from two women who died of eclampsia and one who miscarried at five months have shown that the liver, spleen, kidney and fetus contain almost no anterior pituitary-like principle or estrogenic material. The authors concluded that the excessive amounts of anterior pituitary-like principle previously reported by them in the blood and urine of toxemic and eclamptic women, as well as the tendency toward low levels of estrogenic substance, have their origin in the placenta. They suggest that a continued overproduction of anterior pituitary-like principle by the placenta is probably a related factor and possibly causal in the etiology of late pregnancy toxemia and eclampsia.

Granulosa Cell and Brenner Tumors of the Ovary.—Bland and Goldstein review the available literature regarding granulosa cell tumor of the ovary and the Brenner tumor. Individual summaries of 160 cases of the granulosa cell tumor and sixty cases of the Brenner tumor are tabulated. These, together with eighty-five cases of granulosa cell tumor reported in groups, make a total of 311 cases. Clinically, the granulosa cell and Brenner tumors are relatively benign. Only occasionally do they break through the capsule, recur or metastasize. The granulosa cell tumor occurs most frequently after the menopause. Seventy of the growths reported developed in women aged 50 years or more. Likewise, it was noted that the Brenner tumor occurred in thirty-six women well past the menopausal years. Seven cases of granulosa cell tumor, however, occurred in children less than 10 years of age. Uterine bleeding (menorrhagia, metrorrhagia) was the most common symptom manifested by patients with the granulosa cell tumor. Of the 117 patients in whom symptoms were described, 60 per cent complained of this symptom. The Brenner tumor does not seem to be associated with conspicuous symptoms. Granulosa cell tumors occurring in children are prone to induce precocious sexual development. A personal case of a granulosa cell tumor arising in a child 7 years of age, who underwent marked sexual development, is presented. Data concerning the final outcome were available in ninety-six cases of the granulosa cell tumor and in thirty-nine cases of the Brenner tumor. Forty-two patients with the granulosa cell tumor were reported well for periods varying from one to ten years after operation, while twenty patients died at varying periods following operation. Four of these patients succumbed from metastases within one year after removal of the neoplasm. Twenty-seven patients in whom the Brenner tumor was found were known to be well at varying periods following operation. Six died within one year after operation. One patient of this group died from metastases.

West Virginia Medical Journal, Charleston

31: 293-340 (July) 1935

Management of Psychoneurotic by the General Practitioner. M. I. Mendeloff, Charleston.—p. 293.

Relationship Between Urinary Pathology and Abdominal Symptomatology. E. Hess, Erie, Pa.—p. 296.

The Osteochondritides. H. A. Swart, Welch.—p. 304.

Meaning of Hallucinations. J. K. Hall, Richmond, Va.—p. 306.

Reduction of Premature Infant Mortality. S. H. Clifford, Boston.—p. 311.

Postoperative Pulmonary Complications. W. V. Wilkerson, Highcoal.—p. 315.

Neoplasms and Cysts of Dorsum of Nose: Case Report. E. C. Hartman, Parkersburg.—p. 322.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Bristol Medico-Chirurgical Journal

52: 83-142 (Summer) 1935

Men Midwives of the Past. M. H. Phillips.—p. 83.
Eczema and Dermatitis. N. Burgess.—p. 103.
Medical Treatment of Hyperthyroidism. J. I. Noble.—p. 113.

British Journal of Radiology, London

8: 403-466 (July) 1935

Cholecystography: Review in Full. A. C. Mooney.—p. 403.
Measurement of Dosage and Intensity Distribution in Radium Teletherapy Unit at Westminster Hospital. H. T. Flint and C. W. Wilson.—p. 426.
"Upright" Radiography, with Especial Reference to Investigation of Accessory Nasal Sinuses. H. E. Yorke.—p. 439.
Deep Effect and Localization in Short-Wave Condenser Field. F. Nagelschmidt.—p. 449.
Chondro-Osteo Dystrophy. F. C. Golding.—p. 457.

British Journal of Tuberculosis, London

29: 127-190 (July) 1935

Is the Delicate Child More Likely Than the Strong One to Grow into the Adult Consumptive? E. Ward.—p. 128.
Tuberculosis in China. G. A. M. Hall.—p. 132.
Distribution and Comparative Morbid Anatomy of Tuberculosis in Captive Animals. A. E. Hamerton.—p. 145.
B C G Vaccine and Its Practical Application. K. N. Irvine.—p. 152.
Some Reflections on Thoracoplasty. W. Jullien and F. C. Ecot.—p. 159.
Value of Triboulet Reaction in Intestinal Tuberculosis. H. J. Robinson and D. B. Cruickshank.—p. 164.

British Medical Journal, London

2: 99-146 (July 20) 1935

*Acute Rheumatism and Its Results. K. D. Wilkinson.—p. 99.
Healing of Tuberculous Cavities. L. S. T. Burrell.—p. 102.
Temperament and Digestive Disorders. M. Culpin.—p. 102.
Industrial Dermatoses, with Especial Reference to Sociological Aspects. E. Graham-Little.—p. 107.
*Clinical Interpretation of the Arneth Count. C. J. Young.—p. 109.
Anesthesia for Tonsillectomy. A. P. Gorham.—p. 112.

Acute Rheumatism and Its Results.—Wilkinson states that rheumatic inflammation, whenever it appears, produces a characteristic microscopic lesion—the submiliary focus. It is common in cardiac muscle, pericardium, endocardium, synovial and subcutaneous tissues and is found in the adventitia and media of arteries in all parts of the body. The typical focus shows four distinct points in its structure: a fibrinous matrix, certain large multinucleated cells, plasma cells or fibroblasts and an aggregation of leukocytes—darkly staining mononuclear cells. At first the nodule shows an aggregation of lymphocytes and plasma cells, later the characteristic multinucleated cells appear, and finally the lesion is replaced by a patch of fibrous tissue. These foci are always accompanied by more or less marked changes in the parenchyma of the tissue invaded and produce a considerable degree of vascular proliferation and hyperemia. In the more chronic forms of acute rheumatism the degree of fibrosis of the myocardium may be truly astonishing. It is of the greatest importance to realize that even in the mildest case in which the myocardium is involved the endocardium may escape; when it is damaged, with consequent valvular defect, the lesion is preceded by changes in the valve leaflets, and the valves are not directly infected from the blood in the chambers of the heart. The mitral valve is most frequently, and the aortic valve quite commonly, damaged, while the tricuspid and pulmonary valves are relatively seldom attacked. Damage is the result of both stresses and vascularity. The relatively avascular pulmonary valves, which sustain comparatively little stress, escape, while the vascular and heavily stressed mitral valve is most seriously and most often involved. Newman has calculated that 0.8 per cent of all elementary school children have rheumatic cardiac disease. Coombes showed that about 40 per cent of all heart disease was rheumatic, that the average rheumatic cardiac patient lived to 28½ years and that only 7 per cent of such patients attained the age of 50. He also showed that nearly half the children who acquire rheumatism before the age of 5 years develop serious cardiac damage, while only a fourth of those who develop rheumatism after 10 years of age become cardiac patients.

Clinical Interpretation of Arneth Count.—While it is well established that infections tend to produce a shift to the left in the Arneth count, Young observed in the course of clinical work that the count sometimes fails to show this shift in acute infections and that it may show a left handed shift in the absence of infection. Such exceptions to the rule detract considerably from its clinical utility. His observations indicate, however, that the apparent failure to conform to expectation is to be associated with the percentage method of recording the count and that, by expressing it in absolute figures per cubic millimeter of blood, errors in its clinical interpretation can generally be avoided. A normal polymorphonuclear output may occur in the presence of infection, notably in undulant fever. In addition to infections, left handed percentage counts may occur in agranulocytosis and in hypersplenism. Right handed percentage shifts may occur after inflammatory reactions, as well as in certain other conditions. An absolute increase in the polymorphonuclear output is necessary for the interpretation of a count as evidence of infection. An absolute increase in output and an absolute reduction due to accelerated removal are the best evidences of inflammatory activity, but the latter change is not always present.

East African Medical Journal, Nairobi

12: 99-126 (July) 1935

Some Sidelights on Early Medical History in East Africa. H. A. Boedeker.—p. 100.
Human Incidence of Brucella Infections in Cattle Bearing District of Tanganyika Territory as Determined by Agglutination Tests. D. E. Wilson.—p. 108.
Advance Stage of Complete Inversion of Uterus in Kikuyu Woman. R. H. Wiseman.—p. 111.

Edinburgh Medical Journal

42: 393-444 (Aug.) 1935

Sir Edward Sharpey-Schafer and His Contributions to Neurology. C. S. Sherrington.—p. 393.
Observations on Blood Pressure in Healthy Adult Males. P. L. McKinlay and A. B. Walker.—p. 407.

Journal of Physiology, London

84: 367-468 (July 24) 1935

Reflex Regulation of Cerebral Blood Flow and Cerebral Vasomotor Tone. J. J. Bouckaert and C. Heymans.—p. 367.
Observations on Binocular Fusion and Rivalry. R. S. Creed.—p. 381.
Effect of Hemorrhage of Varying Degree on Blood and Plasma Volume, on Blood Sugar and on Arterial Blood Pressure. J. D. Robertson.—p. 393.
*Some Immediate Effects of Reduced Cooling Powers on Water Balance and Related Effects in Human Subjects. D. H. K. Lee and A. G. Mulder.—p. 410.
Relation Between Metabolic Processes and Ventricular Electrogram. A. S. Dale.—p. 433.
Effect of Liver Feeding in Relation to Oxygen Want. H. B. Parry.—p. 454.
Elimination of Xylose, Creatinine and Urea by Perfused Mammalian Kidney. A. Hemingway.—p. 458.

Effects of Reduced Cooling Powers on Water Balance.—Lee and Mulder kept male subjects who had refrained from taking food or water for twelve hours at rest during a period of some six and one-half hours on each of three occasions in a room with different atmospheric conditions. A standard meal and a standard amount of water were administered at stated times. A "basal level" of urinary volume of from 15 to 30 cc. an hour was reached during the ensuing three hours in a normal environment. In a hot environment this "basal level" was lowered to from 8 to 15 cc. an hour. This is taken to illustrate the limitation of the concessions allowable to hydration functions at the expense of excretory functions. It was possible to differentiate two fairly constant variations in sweat excretion: (1) a low initial rate and (2) a burst of sweating after water consumption. Psychic factors exert a strong influence on sweating. There is a definite burst of sweating, often profuse in amount, when water is swallowed. This appears to be partly reflex, partly absorptive, in origin. The total amount of sweat lost bears a marked relationship to the humidity of different environments of fairly equivalent "effective temperature." The difference in dehydrating power of the dry and humid environments was reflected in the maximal change in serum-protein percentage, which in the hot wet room was little more than half (7.7 per cent) that in the hot dry room (11.3 per cent).

The blood serum among other body fluids bore a disproportionate amount of the total dehydration (i. e., after six hours of exposure). This disproportion was greater in the hot wet than in the hot dry environment. There was some confirmation of the observation that the cutaneous chloride excretion increases with the length of the exposure, at least during the first four hours. The average concentration in the sweat was low (from 0.2 to 0.25 per cent). Under the conditions of these experiments there was no inability on the part of the body to retain a liter of administered water.

Lancet, London

2: 173-232 (July 27) 1935

Infection and Its Control in Children's Wards. E. H. R. Harries.—p. 173.
Depression of Muscle Tonus as Cause of Atelectasis, Failure of Circulation and Other Postoperative Sequels. Y. Henderson.—p. 178.
Torsion of Spermatic Cord in Infancy. G. F. Langley.—p. 181.
Squint Training Clinic of the L. C. C. M. Thornett-Johnson.—p. 183.
*Alkalosis Arising in Treatment of Peptic Ulcer. W. Oakley.—p. 187.

Alkalosis Arising in Treatment of Peptic Ulcer.—Oakley believes that alkalosis often passes unrecognized. He has collected from the wards of a general hospital seven cases in which treatment was being given for peptic ulcer, which show the necessity of keeping in mind the possibility that alkalosis may develop in any patient taking alkalis regularly, even in moderate doses. Although the dosage of alkali does not vary greatly in the different wards, five of the cases were diagnosed by one physician or his assistants. It is therefore probable that many cases pass undiagnosed either to recovery or (more probably) to death. Six of the patients were men. Symptoms are numerous and varied; the most characteristic are anorexia, headache, irritability and changes in mentality, nausea, vomiting, aching pains and twitching in the muscles of limbs, and weakness, which may amount to prostration. Flushing and perspiration may be present; in severe cases, slow respiration rate, rapid pulse, tetany and even fits may precede the onset of coma, which is usually fatal, the patient dying uremic. The tongue is dry and furred, and, apart from muscular tenderness and urinary changes, the principal signs are those of increased neuromuscular excitability; these include brisk reflexes, muscular twitchings and occasionally latent or frank tetany with carpopedal spasms. Incontinence may complicate severe cases. The urine is typically increased in amount and alkaline in reaction, and contains protein and granular and hyaline casts, red and white blood cells being observed less constantly. The urine may resemble that of acute nephritis. In any suspected case all alkalis should be withheld and the alkali reserve and blood urea estimated. If these are raised, acid should be given in the form of ammonium chloride (from 1 to 1.3 Gm.) or acid sodium phosphate (from 2 to 2.6 Gm.) three times a day after food, until the alkali reserve, which should be estimated daily, has returned to normal limits. The protein intake should be limited to about 40 Gm. a day and all food given should be in fluid or semisolid form, careful attention being paid to the condition of the mouth and intestine. When treatment is given along these lines, recovery should occur in all but the most severe cases; but symptoms, such as pains in the legs, may persist for several weeks. It is unwise to perform any operation until the blood urea has been normal for some days.

Medical Journal of Australia, Sydney

1: 793-822 (June 29) 1935

Some Early Medical Men of Western Australia. F. I. Bray.—p. 793.
The Autonomic Nervous System. H. J. Wilkinson.—p. 801.

2: 1-32 (July 6) 1935

Premedication for Local Anesthesia. C. E. Corlette.—p. 1.
Premedication in General Anesthesia. W. I. T. Hotten.—p. 5.
Use of "Nembutal" in Childbirth. W. J. Rawlings.—p. 12.
Pathogenicity of Dermanyssus Avium et Gallinae and of Trichomes in the Human Being. H. Lawrence.—p. 16.

2: 33-68 (July 13) 1935

The Hospital Problem in Western Australia. R. H. Crisp.—p. 33.
Remarks on Pyelitis and Its Medical Treatment. A. R. Southwood.—p. 35.
Gastric Ulcer from the Surgical Point of View. H. Bullock.—p. 40.

Journal de Chirurgie, Paris

46: 1-160 (July) 1935

Robert Proust. A. Gosset.—p. 3.
*Urgent Indications for Operation in Recent Closed Traumatic Lesions of Skull and Brain. A. Jentzer.—p. 23.
Intercostal-Radicular Anastomosis in Vertebral Traumatisms with Section of Lumbar Medulla. A. Chiasserini.—p. 54.

Traumatism of Skull and Brain.—Jentzer discusses the effect of operation in cranial traumatisms based on the records of 837 cases from 1914 to 1934. There were 366 patients with cerebral contusion who recovered under nonoperative treatment. Seven died in spite of conservative treatment and two in spite of operative intervention. Two hundred and thirty-three patients with cranial fracture recovered under conservative treatment, thirty-nine with fracture recovered after operation, thirty-five died in spite of operation and seventy-three died without operation. There were eighty-two cases of fracture which could not be used for various reasons. From the study of these cases he concludes that the anamnesis can never be sufficiently complete to dictate the therapeutic procedure. In more than 50 per cent of the fractures, some of a severe character, such as slow pulse and hyperpyrexia, recovery occurred without intervention. Indications for operation are given by the succession of physiopathologic phenomena rather than by any one set of signs. In the severe cases, immediate operation is indicated. This is based on the enormous anatomic lesions observed in 117 necropsies. Such lesions could not be expected to heal without surgical help. In some, microscopic traumatisms develop toward neurologic sclerosis. The changes in the choroid plexus, the different effects of hemorrhage, the sympathetic disorders (congestion, edema, anemia) and the silent lesions might all be helped by early trephining. The author concludes that death is not produced by lesions of the hemispheres alone, of the protuberance, of the peduncle or of the bulb and by hemorrhages, but that cerebral edema, pulmonary lesions and emboli are common fatal complications.

Schweizerische medizinische Wochenschrift, Basel

65: 693-716 (Aug. 3) 1935

Heredity, Race Hygiene and Eugenics. A. Werthemann.—p. 693.
Causes of Death in Sepsis Lenta. M. From.—p. 698.
Improvement of Cultural Examination of Blood. R. K. Grilichess.—p. 699.
*Relation of Nodose Rheumatism to Juxta-Articular Nodules. S. Bollag.—p. 702.
Hypertension in Disorders of Adrenals. G. Piotrowski and F. Ody.—p. 704.
Consumption of Alcoholic Liquors in Switzerland. V. J. Steiger.—p. 706.

Relation of Nodose Rheumatism to Juxta-Articular Nodules.—According to Bollag, nodose rheumatism is characterized by painless, easily recognizable subcutaneous nodules that vary in size from a lentil to a pea and occasionally are somewhat larger. Though most reports agree that these nodules are usually near the joints, similar formations have been observed also on tendons, cranium, ribs, tibia and pelvis and in other locations. Moreover, nodules on certain internal organs, such as the myocardium and the pericardium, have likewise been brought into relation to nodose rheumatism. In this connection the author calls attention to Aschoff's nodules, which are found in rheumatic myocarditis but which, according to some investigators, may also be classified with nodose rheumatism. In studying the problem of nodose rheumatism, it will be noticed that in the dermatologic literature, or in the literature on tropical diseases, juxta-articular nodules are likewise described. The author points out that in recent years it has been discovered that the so-called tropical juxta-articular nodules are really not a tropical disorder but are of syphilitic nature. The clinical aspects of these syphilitic (dermatologic) juxta-articular nodules do not differ greatly from those of the nodules that are characteristic for nodose rheumatism, but most investigators agree that the two conditions have to be differentiated. The author gives the clinical history of a woman, aged 28, who suffered from recurrent swellings of the joints and in whom nodules were detected on both wrists and behind the ear. The patient had typical Hutchinson's teeth and the Wassermann reaction was once weakly positive, while

later controls were negative. Later, nodules were detected also on other parts of the body. Treatment with a gold preparation improved the articular function and reduced the pain in the joints, and the nodules gradually disappeared. The author points out that the differential diagnosis is extremely difficult in this case, for the nodules may be a manifestation of nodose rheumatism in a person with congenital syphilis or they may be juxta-articular nodules. He emphasizes that, in studying juxta-articular nodules, dermatologists should not overlook the possibility of a nodose rheumatism and internists should not disregard the possibility of a syphilitic nature of the juxta-articular nodules.

Riforma Medica, Naples

51: 1087-1124 (July 20) 1935

*Antimony Stimulation of Reticulo-Endothelial System in Estivo-Autumnal Malaria. R. De Nunno.—p. 1087.
Prophylactic Value of Antisyphilitic Ointments. A. Oro.—p. 1092.
Postoperative Contralateral Phlebitis Due to Intervention on Right Side of Abdomen: Four Cases. V. Bernabeo.—p. 1093.

Antimony Stimulation of Reticulo-Endothelial System in Estivo-Autumnal Malaria.—In a preliminary report, De Nunno concludes that the intravenous injections of antimony and potassium tartrate, given to rabbits in doses corresponding to those used in human beings, provoke a stimulation of the reticulo-endothelial cells that is more marked if the animals are given the largest therapeutic doses that can be given to human beings. Tartrated antimony has the same action on the reticulo-endothelial cells of human beings, as proved by the author by the examination of the splenic pulp before and after its administration. The treatment consists in intravenous injections of a 1 per cent solution of antimony and potassium tartrate given every other day in increasing doses of from 1 to 14 cc. of the solution up to a total quantity that varies, according to the more or less rapid disappearance of the plasmodium in the splenic pulp, between 175 and 213 cc. for the two courses of injections. The first few injections are followed by a mobilization of plasmodia, which appear in the blood in endoglobular and crescent forms and provoke the development of more or less typical malarial febrile spells. The size of the spleen diminishes from the third or the fourth injection and is normal at the end of the treatment. In fourteen adult patients suffering from estivo-autumnal malaria that had resisted quinine, plasmochin and atabrine treatments, the antimony treatment resulted in the recovery of thirteen. All were carriers of plasmodium praecox, which disappeared from the spleen after the treatment. One patient discontinued the treatment because of intolerance when he had received 162 cc. of the solution. By that time the size of the spleen was reduced and recovery occurred three weeks later by the administration of plasmochin and quinine as complemental treatments. The intravenous injection of antimony and potassium tartrate, if given before or during the development of a malarial spell, does not control its development. The therapeutic effect of the treatment is due to the action of antimony and potassium tartrate on the reticulo-endothelial system, both by stimulating the proliferation of phagocytes and by acting, after its accumulation in the cytoplasm of the reticulo-endothelial cells, on the phagocyted plasmodia. The author advises the treatment in chronic malaria in order to ascertain its indications and efficacy from its results in groups of patients larger than his group.

Semana Médica, Buenos Aires

42: 149-224 (July 18) 1935. Partial Index

Systolic Murmur of Third or Second Left Intercostal Space in Hyperthyroidism. P. Cossio, E. B. del Castillo and O. Fustinoni.—p. 149.
Clinical Prognosis of Myocardial Infarct. G. Bosco.—p. 158.
Esthetic Phrenicectomy. G. H. Dickmann.—p. 160.
Abortion Following Sexual Trauma. P. E. Borrás.—p. 172.
*Rheumatic Fever in Etiology and Pathogenesis of Painful Valgus Talipes. G. Costa Bertani.—p. 176.
*Effect of Magnesium Chloride Intravenously Injected in Cases of Venereal Papilloma and Warts. A. A. Fernandez and J. Capurro.—p. 192.
Liphoid Nephrosis: Case. A. N. Accinelli.—p. 196.

Rheumatic Fever in Painful Valgus Talipes.—According to Costa Bertani there is a type of painful valgus talipes of rheumatismal origin that occurs in patients regardless of age. The author reports fifteen cases in which the rheumatismal etiology was indubitable. The patients ranged in age between 8 and 43. This explanation of the pathogenesis of the condition is the theory of an infectious (rheumatic) arthritis at the tibiotarsal and metatarsal joints, followed by distention of the deltoid and calcaneoscaphoid ligaments and of the muscles and tendons of the internal edge of the arch of the foot, which result in relaxation of Chopart's joint and collapse of the internal edge of the arch. These changes determine the rupture of the normal relations of the joints of the foot and, if the factors of standing or walking are added, a traumatic arthritis develops. Traumatic arthritis is the cause of the contracture and secondary changes that follow. Rheumatic painful valgus talipes may occur from a primary localization of the virus of rheumatic fever exclusively at the heel and the joints of the foot, or as the secondary phase of a painless valgus talipes of rheumatic origin. In either case the mechanism of its production is the same. The author does not believe that standing or walking alone causes painful valgus talipes. Neither does he agree that this type of talipes should be termed "flat rheumatic talipes," because the occurrence of painless flat valgus talipes is frequent, while the feet are never flat in cases of rheumatic painful valgus talipes. By the use of orthopedic arch supports as soon as talalgia (the first symptom of painful valgus) appears the pain disappears, the patient regains his functional capacity and further deformity of the foot is prevented.

Magnesium Chloride in Treatment of Venereal Papilloma and Warts.—Fernandez and Capurro advise the administration of intravenous injections of magnesium chloride in the treatment of venereal papilloma and warts. They used a 40 per cent solution of anhydrous magnesium chloride in water or in physiologic solution of sodium chloride; that is, a solution in which each cubic centimeter of the solvent contained 0.4 Gm. of the solute. They begin with injections of 0.05 or 0.1 Gm. and increase the dose according to the age and tolerance of the patient, if possible, up to 1 or 2 Gm. for each injection in adults. The number of injections varies with the evolution of the disease during the treatment and the reaction of the patient to the drug. After a number of injections, which in the cases of the authors varied from ten to forty, an interval of rest without injections is allowed. Improvement manifests itself during the treatment and generally recovery is completed during the period of rest. This is due to the cytophylactic properties of the drug, which last for some time after the injections are given. If satisfactory results are not obtained from the first series of injections, the treatment may be repeated. The authors report the results of the treatment in a group of twenty-four patients suffering from venereal papilloma or warts. In fifteen patients complete recovery was obtained, five were improved, in four the condition remained unchanged and the rest of the patients did not report for further observation after having received one or more series of injections. Because of the cytophylactic effects of the drug and of the improved condition of the patients when they discontinued the treatments, the authors believe that their recovery was probable.

Klinische Wochenschrift, Berlin

14: 1089-1128 (Aug. 3) 1935. Partial Index

Diparameteric Consideration of Pathergic Process and Principle of Pathergometry. F. von Gröer.—p. 1094.
Action Mechanism of Estrogenic Hormone: Clinical Observations on Position of Hypophysis. P. Hauptstein.—p. 1103.
*Disturbances in Water and Mineral Exchanges in Addison's Disease. G. Marañón and J. A. Collazo.—p. 1107.
Circulating Quantity of Blood Before and After Mercury Diuresis. S. Goldhammer, G. Leiner and D. Scherf.—p. 1109.

Water and Mineral Exchanges in Addison's Disease.—Marañón and Collazo investigated the following problems in patients with Addison's disease: the content of the blood, the water content of the muscles, the ion content of the blood, the action of adrenal cortex extract on the water and electrolyte content of the blood, the water elimination and the value of sodium chloride in the treatment. They found that in patients with chronic adrenal insufficiency there exists a more or less pronounced dehydration, which is demonstrable in the blood plasma as well as in the muscular tissues. They are convinced

that this dehydration plays an important part in the terminal manifestations of the disease, for it is connected with the severe acidosis that is typical in the last stages of the disease. The causes of the dehydration are supposedly quite complicated. They are doubtless influenced by the loss of glycogen from the liver and also by disturbances in the mineral exchange, the most noteworthy sign of which is a disturbance in the potassium-sodium equilibrium; namely, an increase in the potassium ions and a relative decrease in the sodium ions. The injection of adrenal cortex extract produces in these patients an increase in the water retention and aids in reestablishing the disturbed potassium sodium equilibrium. The effect of sodium chloride on adrenal insufficiency in adrenalectomized animals, as well as observations on patients with Addison's disease, induced the authors to give sodium chloride in connection with adrenal cortex extract. The authors found that the addition of sodium chloride counteracts the dehydration, reduces the severity of the symptoms and improves the general condition of the patients with Addison's disease.

Münchener medizinische Wochenschrift, Munich

82: 1185-1224 (July 26) 1935. Partial Index

Remarks on Treatment of Hypertrophy of Prostate. M. Kirschner.—p. 1185.
*Cause of Arteritis. W. Braeucker.—p. 1186.
*Scarlet Fever Blanching Phenomenon—Calcium Blanching Phenomenon—Pseudoblanching Phenomenon. F. Gerth and F. Trautmann.—p. 1188.
Management of and Fatalities in Delivery of Twins in Home. C. Holtermann.—p. 1191.
Anesthesia in Small Interventions on Female Genitalia. Vilma Janisch-Raskovié.—p. 1195.

Cause of Arteritis. — Braeucker points out that the first detailed description of an arterial inflammation was given in 1879 by von Winiwarter, who designated the conditions as endarteritis obliterans. Later several other investigators corroborated the observations made by von Winiwarter. Buerger studied vascular inflammations on a large material. He did not place the same stress on the changes of the intima as von Winiwarter had done but designated the disorder as thrombo-angiitis obliterans because in the beginning stage of the disorder there exists only an inflammation of the vascular wall, which is later followed by a thrombosis. The author discusses the histologic aspects of thrombo-angiitis obliterans (Buerger's disease) and mentions the various theories that have been advanced regarding the pathogenesis of this disorder. Several investigators have stated that thrombo-angiitis obliterans is related to infectious rheumatism, but this theory has been rejected by leading pathologists and clinicians. Some authorities think that the disorder may be caused by different factors, while Buerger believed that it is an infectious disease. To be sure, Buerger did not succeed in finding the causal organism, but he succeeded in transmitting the disease and, at any rate, he thinks the disease occupies a unique position, and a number of clinicians are inclined to agree with him. The author points out that from Buerger's disease in the restricted sense of the word there can be differentiated a number of other vascular inflammations, such as those developing in typhus, cholera, scarlet fever and other infectious diseases, as well as those developing after frost bite and traumas. He gives the detailed description of a case in which a vascular inflammation developed after a trauma. The inflammation was localized especially in the external layers of the artery. Thus the anatomic pathologic aspects were not those characteristic for Buerger's disease. Moreover, the clinical symptomatology was not like that of thrombo-angiitis obliterans. In addition, the author observed two other cases in which vascular inflammations developed after traumatic injuries. He considers it unjustified to ascribe such posttraumatic forms of arteritides chiefly to constitutional factors. He concedes that such factors may be involved, but he emphasizes that the trauma is the most important factor, just as the infection is the most important factor in the forms of arteritides that develop after infectious diseases.

Scarlet Fever Blanching Phenomenon. — Gerth and Trautmann, in their discussion of the scarlet fever blanching phenomenon, show that this sign is produced by injecting intracutaneously from 3 to 5 cc. of blanching serum at a suitable site within the region of the scarlet fever exanthem and watching the results after from six to eight hours. If the outcome is positive, the exanthem disappears over an area varying in size from that of a quarter dollar (24 mm.) to that of the palm of the hand. There is evidence that the scarlet fever blanching phenomenon is caused by an immunologic property of the injected blood serum. Although the specificity of the scarlet fever blanching phenomenon is generally accepted, there are nevertheless certain aspects that induced the authors to make further investigations of its mechanism. They discuss the so-called calcium blanching phenomenon and Glanzmann's assertion that the blanching phenomenon may be positive in exanthems that are not due to scarlet fever. The authors studied the phenomenon in fifty-eight cases, employing blanching serum as well as calcium and giving their attention also to the so-called pseudoblanching phenomenon. In summarizing their opinion of the present status of the scarlet fever blanching phenomenon they state that: 1. The scarlet fever blanching phenomenon is a specific reaction. 2. The calcium blanching phenomenon is the result of vasomotor actions of the calcium salt; it is not suited to replace the serum blanching phenomenon. 3. In some instances, undesirable secondary effects of the blanching serum may produce a pseudoblanching phenomenon; that is, a nonspecific reaction in the form of a centrally slightly elevated erythema with a lighter peripheral zone. The authors describe a case in which a pseudoblanching phenomenon developed. In this woman scarlet fever could be excluded on the basis of the anamnesis, the onset and the course of the disease, and the absence of eosinophils from the blood at the most severe stage. The fact that the patient's serum produced blanching phenomena in scarlet fever exanthems was a further proof that the disorder was not scarlet fever; it was found to be a mercury dermatitis.

Zentralblatt für Gynäkologie, Leipzig

59: 1809-1872 (Aug. 3) 1935. Partial Index

Pregnancy and Delivery in Hypophyseal Obesity. K. Heyrowsky.—p. 1810.
Spondylolisthesis and Course of Delivery (Case of Spontaneous Delivery in Case of Spondylolisthetic Pelvis). H. Kirchhoff.—p. 1813.
*Intra-Operative and Postoperative Circulatory Weakness Following Lumbar Anesthesia. E. Preissecker.—p. 1819.
Casuistics on Enormous Loss of Blood. W. Jelinek.—p. 1824.
*Improved Method of Artificial Detachment of Placenta. R. Budimlié.—p. 1827.

Circulatory Weakness Following Spinal Anesthesia.— Preissecker points out that, although great care is taken to detect an impairment of the heart before spinal anesthesia is decided on, there occur nevertheless cases of collapse. This type of collapse is not the result of cardiac failure but is caused by deficiencies in the peripheral circulation; that is, it is a vascular shock. The author shows that this vascular shock is probably the result of sensitization to protein, for in women with diseased genitalia, parametritis, tumors of the adnexa, carcinoma or bleeding myomas, protein decomposition takes place, and sensitization and then an impairment of the peripheral circulatory system is quite likely. In such sensitized persons spinal anesthesia may prove to be too much of a tax on the circulation, particularly if in the course of the operation more decomposition products of protein enter the circulation. The author gives his attention to the forms of collapse that develop a number of hours or even several days after the operation. This form of collapse is not the result of the spinal anesthesia as such, for the effect of the anesthesia has completely disappeared after a few hours. He emphasizes that this type of collapse is the result of autointoxication or of an allergic condition. An increase in the temperature after operation indicates that decomposition of protein is taking place. That a collapse does not result in all cases the author ascribes to the fact that the sensitivity for parenteral protein digestion varies in the different patients; it is determined not only by the patient's constitution but also by the preoperative condition. The author shows that gynecologic operations, more than most other interventions, involve the decomposition of enormous quantities of protein (great vascularity of the region, bruising of tissues with large clamps, ligation of stumps and so on), which enter the circulation.

To be sure, he admits that other forms of anesthesia will probably not reduce the danger of a peripheral circulatory shock, but he thinks that the incidence and mortality of this type of shock might be reduced if there were a method for the early recognition of a latent tendency to collapse. He thinks that the preoperative determination of the amount of protein cleavage products in the blood, or the determination of the reaction capacity of the organism by means of the cantharidal blister, might be of value. He emphasizes that preoperative digitalization of the patients is without avail, for the prevention of central collapse does nothing to prevent peripheral collapse. He thinks, however, that the use of vascular tonics that favor a backflow to the heart will be of help. He warns against protein shock therapy in patients in whom a later operation is probable and he also advises that alkaloids and barbituric acid preparations should be used sparingly. It is essential that in the course of the operation bruising of tissue be avoided as much as possible.

Artificial Detachment of Placenta. — Budimlić injected into fresh placentas through the umbilical vein solutions of various astringents and watched their action on the placenta. He obtained the best results with a 0.45 per cent solution of alum. He describes the method as he employs it to effect detachment of the placenta. In 1 liter of boiling distilled water he places 4.5 Gm. of crude alum, lets the solution cool to 39 C. and then injects at once 300 cc. of this solution into the umbilical vein after it has been closed with a Péan clamp. If detachment of the placenta does not follow within fifteen minutes, which is rarely the case, an additional 50 or 80 cc. of the solution is injected. As a rule it is possible to wait for an hour or even longer for the complete detachment of the placenta, because the uterine hemorrhage usually ceases following the injection. The author made the injection into the umbilical vein as a rule forty-five minutes after the delivery; but, in cases in which the hemorrhage threatened the mother's life, the injection was made immediately after the delivery. He employed the method successfully in nineteen cases, in eight of which manual detachment had been necessary in previous deliveries. He points out that, if manual detachment becomes necessary in spite of the injection, the difference in the consistency of uterus and placenta (the placenta is harder as the result of the injection) facilitates the manipulation considerably. He emphasizes that the method is quite helpful for the practitioner, for all that is needed is a supply of 500 cc. of alum solution, a syringe of 150 cc. capacity and a Péan clamp. Because the solution is hypotonic, the injection is without danger and he considers it superior not only to the manual detachment but also to Credé's manipulation, for the latter method may be followed by inversion of the uterus or by collapse.

Nederlandsch Tijdschrift voor Geneeskunde, Haarlem

79: 3827-3938 (Aug. 10) 1935

Ulcerous Tuberculids. E. Zurhelle.—p. 3828.
*Hypochromatic Anemia with Symptoms in Ocular Fundus. A. P. Daniels and C. O. Roelofs.—p. 3835.
*Hirsau Treatment of Parkinsonism. J. J. Wuite.—p. 3849.
Surgical Treatment of Trigeminal Neuralgia. C. Klein.—p. 3855.
Difficulties with Acid-Fast Saprophytes in Cultures of Tubercle Bacilli. A. Charlotte Ruys.—p. 3859.
Vegetative Syndrome During and After Influenza. A. M. Meerloo.—p. 3863.
Malignant Hypertension with Cerebral Complications. A. M. Meerloo.—p. 3868.

Hypochromatic Anemia with Symptoms in Ocular Fundus.—Daniels and Roelofs describe two cases of secondary hypochromatic anemia. Symptoms common to the two patients were inflammation of the optic papilla, temporary disturbances of voluntary movement, migraine and vomiting. The patients also showed marked changes in the fundus of the eyes resembling those found in brain tumor. The neurologic symptoms coincided with a symptomatic migraine and were considered the consequence of a spasm of the blood vessels caused by the anemia. The changes in the fundus of the eyes were explained as resulting from contractions of the retinal vessels owing to the direct influence of the anemia. The literature concerning similar cases is discussed and in many respects confirms the hypothesis. The success of treatment of the anemia on the other symptoms supported the theory that the anemia alone was the primary cause.

Treatment of Parkinsonism.—Wuite describes the technic of the Hirsau sanatorium treatment or parkinsonism as reported by Anna Kleemann. The patient is placed in a luke-warm bath in the morning, during which time passive movements are made with the limbs. After the bath, the limbs are massaged and the patient rests. In the evening he is given 0.25 mg. of atropine sulphate in 0.5 per cent solution. The second day the dose is doubled and the third day tripled. After the third day the dose is given every three hours, preferably at 6 a. m., 2 p. m. and 10 p. m. Dryness in the throat is no contraindication to an increase in dosage. If disturbances, such as vertigo, sensations of heat, palpitation of the heart and gastric complications, occur, the dosage remains the same until these symptoms disappear. The maximal dose varies according to the individual. When the limit of tolerance has been reached, it is indicated by such symptoms as dulness, headache, apathy and sleeplessness. Physical treatment simultaneously administered consists in daily baths, massage, active and passive movements of the limbs and physical labor. The first symptoms to disappear during treatment are vegetative symptoms, such as excessive salivation, tear flow and secretion of sebum, along with disturbances of the muscular tonus, such as stiffness, slowness and defects of speech and ambulation. The last to disappear are the involuntary movements (tics and tremors) and the psychic disturbances (slowness, apathy, blocking of thought and depressive psychoses). According to the author the optimal atropine dosage should be determined by the disappearance of the symptoms of the motor sphere, particularly those of the muscular tonus. Treatment should be administered in an institution with all facilities at hand.

Ugeskrift for Læger, Copenhagen

97: 747-768 (July 18) 1935

*Experiences with Treatment of Diabetes with Insulin-Epinephrine. V. Clausen and M. C. Lottrup.—p. 747.
*Insulin-Epinephrine Treatment According to Clausen. T. T. Andersen.—p. 751.
Tabetic Arthropathy of Column: Two Cases. C. Krebs.—p. 752.

Treatment of Diabetes with Insulin-Epinephrine.—Clausen and Lottrup, who found that the addition to insulin of minimal amounts of epinephrine causes a protracted resorption of insulin injected subcutaneously without otherwise changing the effect of the insulin and without unpleasant by-effects, illustrate the advantages of the method in five of the twenty-five cases in which this treatment was used. The first two patients, whose blood sugar varied greatly with two injections of insulin daily and who were often at the point of hypoglycemia, improved on the use of insulin-epinephrine 1:50,000 for both injections and still more when insulin-epinephrine 1:25,000 was used for the evening injection. For such patients the authors give most of the carbohydrate from three to four hours after the morning injection and a moderately small amount with the evening meal. So far as is feasible an interval of twelve hours between injections is advised. The next two cases show that with insulin-epinephrine it may in some instances be possible to change from two injections to one daily. As little carbohydrate as possible is then given with the evening meal. The fifth case shows that with insulin-epinephrine good results may sometimes be attained in a few days.

Insulin-Epinephrine Treatment According to Clausen.—Andersen says that of seventeen diabetic patients under ambulant treatment since January 1935, all given insulin-epinephrine, four are unchanged and thirteen improved. In seven of the thirteen glycosuria has largely or wholly disappeared; nine patients, who before the treatment had hypoglycemic attacks, have since the start of this treatment been free from hypoglycemic symptoms. The only patient still presenting symptoms of hypoglycemia is suffering from epilepsy. The author considers Clausen's method advantageous and well worth using until slowly resorbable insulin is available, and possibly even then if the new insulin proves too expensive.